

# THE EFFECT OF NOISE EXPOSURE ON AUDITORY THRESHOLD, OTOACOUSTIC EMISSIONS, AND ELECTROCOCHLEOGRAPHY

by

Alyson Butler Lake, B.S., Au.D.

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Director of Dissertation: Andrew Stuart, Ph.D.

Major Department: Communication Sciences and Disorders

Noise exposure is the second leading cause of acquired sensorineural hearing loss and is one of the most common occupational and environmental hazards. Examining changes in behavioral thresholds has long been the standard for detection and monitoring of noise-induced hearing loss (NIHL). It has been suggested that electrocochleography (ECochG) could be an additional tool for assessing NIHL. Otoacoustic emissions (OAEs) provide objective information on the integrity of outer hair cell (OHC) function and have also been suggested for evaluating damage due to noise overexposure. The broad experimental question was: What is the effect of short-term narrowband noise exposure, as a function of ear and gender, on cochlear function as measured with behavioral, ECochG, and OAE indices? In Experiment 1, it was of interest to first examine the reliability of ECochG electrode type (i.e., Lilly-TM Wick vs. TIPtrode™) at two stimulus rates (i.e., 7.7/s vs. 77.7/s). Electrode and rate were statistically significant ( $p < .001$ ) predictors of SP and AP responses (i.e., responses were more apt to be present when recorded with the wick electrode at the slow rate). Test-retest reliability was examined with correlation coefficients, linear mixed model analyses of variance, test-retest differences, and Bland-Altman plots. There were

statistically significant correlations ( $p < .05$ ) between initial test and retest for all ECoChG indices (i.e., summing potential [SP] amplitude, action potential [AP] latency, AP amplitude, SP/AP amplitude ratio, and SP/AP area ratio) when using a Lilly TM-Wick electrode and for all ECoChG indices except SP amplitude when testing with a TIPtrode™. Amplitude measures were significantly ( $p < .01$ ) larger when recording with the wick electrode. SP amplitudes were significantly ( $p < .05$ ) larger for the faster rate. AP latency was significantly ( $p < .001$ ) longer for the fast rate. AP amplitudes were significantly ( $p < .05$ ) larger for the slower rate. Both SP/AP amplitude ratio and SP/AP area ratio were significantly ( $p < .001$ ) larger for the fast rate. There was no statistically significant effect of test on any ECoChG indices ( $p > .05$ ). In Experiment 2, auditory threshold differences were examined as a function of ear, gender, and frequency. Significantly ( $p < .0001$ ) larger auditory threshold differences were observed for left ears and for 3000 Hz than 2000 Hz, 4000 Hz or 6000 Hz. Additionally, statistically significant correlations between right ear auditory threshold differences at 3000 Hz and right 2000 Hz pure tone acoustic reflex thresholds ( $p = .04$ ) as well as between left ear auditory threshold differences at 3000 Hz and left 2000 Hz pure tone acoustic reflex thresholds ( $p = .03$ ) and 2000 Hz narrowband noise acoustic reflex thresholds ( $p = .01$ ) were found. Statistically significant main effects of level ( $p < .0001$ ) and frequency ( $p < .0001$ ) were observed for DPOAE I/O functions in Experiment 3. DPOAE absolute amplitude differences were largest for the L1, L2 level of 55, 40 dB SPL and smallest for the L1, L2 level of 65, 65 dB SPL. DPOAE absolute amplitude differences were also smallest for the  $f_2$  frequency of 2051 Hz. A statistically significant gender by frequency interaction ( $p < .05$ ) was also identified. Females generally had larger DPOAE absolute

amplitude differences than males except at the  $f_2$  frequency of 4980 Hz. Finally, Experiment 4 revealed a statistically significant interaction of ear and gender ( $p < .05$ ) for SP amplitude. SP amplitudes were significantly increased for female left ears following noise exposure while female right ears showed essentially no change. Additionally, left ear SP/AP amplitude ratios and SP/AP area ratios were significantly ( $p < .05$ ) increased following noise exposure. In summary, due to the excellent test-retest reliability and easier identification of ECoChG wave components, Lilly-TM Wick electrodes were deemed superior for recording ECoChG. Experiments 2, 3, and 4 revealed that behavioral thresholds, DPOAE I/O functions, and ECoChG showed measureable changes following a 2000 Hz narrowband noise exposure.



THE EFFECT OF NOISE EXPOSURE ON AUDITORY THRESHOLD, OTOACOUSTIC  
EMISSIONS, AND ELECTROCOCHLEOGRAPHY

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by

Alyson Butler Lake

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Alyson Butler Lake

APPROVED BY:

DIRECTOR OF DISSERTATION: \_\_\_\_\_

Andrew Stuart, Ph.D.

COMMITTEE MEMBER: \_\_\_\_\_

Deborah S. Culbertson, Ph.D.

COMMITTEE MEMBER: \_\_\_\_\_

Paul Vos, Ph.D.

INTERIM CHAIR OF THE DEPARTMENT

OF COMMUNICATION SCIENCES AND DISORDERS: \_\_\_\_\_

Jamie Perry, Ph.D.

DEAN OF THE

GRADUATE SCHOOL: \_\_\_\_\_

Paul J. Gemperline, Ph.D.

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## LIST OF SYMBOLS AND ABBREVIATIONS

ABR	Auditory brainstem response
AC	Alternating current
ACOEM	American College of Occupational and Environmental Medicine
ALR	Auditory late response
ANOVA	Analysis of Variance
AP	Action potential
Ca <sup>2+</sup>	Calcium
CDC	Centers for Disease Control and Prevention
Cl <sup>-</sup>	Chloride
cm	Centimeters
cm <sup>3</sup>	Centimeters cubed
CM	Cochlear microphonic
CPA	Cerebello-pontine angle
CN	Cochlear nucleus
daPa	Dekapascal
dB	Decibels
dB(A)	A-weighted decibels
DC	Direct current
<i>df</i>	Degrees of freedom
DPOAE	Distortion product otoacoustic emission
ECochG	Electrocochleography



EEG	Electroencephalogram
$\eta^2$	Eta squared
$\eta_p^2$	Partial eta squared
ET	Extratympanic
$F$	$F$ -ratio
$f_1$	Lower value in Hertz of two paired primary tones
$f_2$	Higher value in Hertz of two paired primary tones
FFT	Fast Fourier Transform
GSI	Grason-Stadler
HC	Hair cell
Hz	Hertz
IC	Inferior colliculus
IHC	Inner hair cell
I/O	Input/output
$K^+$	Potassium
L1	Sound pressure level in dB of the $f_1$ frequency
L2	Sound pressure level in dB of the $f_2$ frequency
LL	Lateral lemniscus
LOC	Lateral olivocochlear
$\mu s$	Microsecond
$M$	Sample Mean
MD	Ménière's disease

MEM	Middle ear muscle
MGB	Medial geniculate body
MLR	Middle latency response
mm	Millimeters
mm <sup>2</sup>	Millimeters squared
mM	Millimolar
mmhos	millimhos
MMN	Mismatch negativity
MOC	Medial olivocochlear
mV	Millivolt
<i>n</i>	Number of cases in a subsample
<i>N</i>	Total number of cases
Na <sup>+</sup>	Sodium
NIDCD	National Institute on Deafness and Other Communication Disorders
NIHL	Noise-induced hearing loss
Ω	Ohm
OAE	Otoacoustic emission
OHC	Outer hair cell
OSHA	Occupational Safety and Health Administration
<i>p</i>	Probability
PTS	Permanent threshold shift
<i>r</i>	Estimate of the Pearson product-moment correlation coefficient

<i>SD</i>	Standard deviation
<i>SE</i>	Standard Error
SL	Sensation level
SOAE	Spontaneous otoacoustic emission
SOC	Superior olivary complex
SP	Summating potential
SPL	Sound pressure level
SRT	Speech recognition threshold
<i>t</i>	Student's <i>t</i> distribution
TEOAE	Transient evoked otoacoustic emission
TM	Tympanic membrane
TPP	Tympanometric peak pressure
TT	Transtympanic
TTS	Temporary threshold shift
TW	Tympanometric width
$\mu\text{V}$	Microvolts
$V_{\text{ea}}$	Ear canal volume
WHO	World Health Organization
$Y_{\text{tm}}$	Peak compensated static acoustic admittance

## CHAPTER I: REVIEW OF THE LITERATURE

### Introduction

Noise exposure is the second leading cause of acquired sensorineural hearing loss after age-related hearing loss and is one of the most common occupational and environmental hazards (Rabinowitz, 2000). Approximately 26 million Americans have hearing loss that may be the result of exposure to noise in either work or recreational environments (National Institute on Deafness and Other Communication Disorders [NIDCD], 2014). Additionally, as many as 16% of teenagers between the ages of 12 and 19 have reported hearing loss that could be attributed to loud noise exposure.

Noise exposure has become a major concern in work environments with 30 million Americans being at risk for work related NIHL (Dobie, 2008). Dobie (2008) suggested that occupational noise has most likely caused 5% to 10% of the hearing loss burden in the United States. It is suspected that non-occupational noise (e.g., hunting) contributes to an additional 6% of the hearing loss burden in the United States (Dobie, 2008). NIHL is not only the most prevalent occupational condition occurring across a wide spectrum of industries, it is also entirely preventable through a hierarchy of controls (American College of Occupational and Environmental Medicine [ACOEM], 2012). These controls are set in place to “prioritize the use of engineering controls over administrative controls and personal protective equipment” (ACOEM, 2012, p. 106).

Noise exposure, in addition to loss in hearing sensitivity, can lead to a reduction in temporal summation, poor frequency resolution and speech discrimination, abnormally rapid loudness growth, and tinnitus in humans. This suggests that not only

is the inner ear affected by intense noise exposure, so are the neural processes of the auditory system (Salvi et al., 1983).

The following literature review will first discuss the anatomy and physiology of the auditory system and the effects of noise on auditory function. There will be a detailed discussion of various assessments of the auditory system with emphasis on the audiometric profile of NIHL. In addition, there will be a brief discussion on the management of noise to include the Occupational Safety and Health Administration (OSHA) and hearing conservation programs. At the conclusion of the literature review, gaps in the current literature and relevant research questions will be presented.

### **Anatomy and Physiology of the Human Peripheral Auditory System**

The peripheral auditory system of humans is comprised of three components: the outer ear, middle ear, and inner ear. This system functions by converting acoustic energy, or sound waves, to mechanical energy, which in turn is converted to hydraulic energy in the inner ear. Ultimately, the physical vibration of the sound wave is transformed to a neural impulse to be processed by the central auditory pathway of the brain. The human auditory system has a frequency range of approximately 10 octaves, spanning from 20 to 20,000 Hertz (Hz; Seikel, King, & Drumright, 2005). The ear is also responsible for performing much finer tasks including the differentiation of small increments in frequency and intensity, listening to a signal embedded within background noise, and listening to extremely rapid sequences of sound. Each component of the peripheral auditory system has a different role in carrying the signal to the central auditory system.

## Outer Ear

The outer ear is comprised of the pinna and the external auditory meatus and can be seen as primarily a collector of sound. The pinna is a cartilaginous flange protruding from the side of the head, which includes the resonant cavity of the concha. Here sound is collected and funneled into the narrower external auditory meatus. The external auditory meatus is approximately 0.7 centimeters (cm) in diameter and 2.5 cm long from the depth of the concha to the lateral surface of the tympanic membrane (TM; Seikel et al., 2005). According to Seikel et al. (2005), the lateral third of the external auditory meatus is cartilaginous and about 0.8 cm long, while the medial two-thirds of the canal is the bony meatus of the temporal bone. The outer ear can only have passive effects on the input stimulus due to the lack of moveable components. The pinna has several important functions including localization of sound in space and capturing of sound energy (Pickles, 2008; Seikel et al., 2005).

**Sound localization.** The most important cues for sound localization include intensity and timing differences in the sound waves at the two ears; however, this does not account for the ability to distinguish in front from behind and above from below. The angling of the pinna contributes to more collection of sound from the front of the head than from the back, aiding in sound localization. Specifically, the raised ridges of the pinna and concha reflect sound waves into the ear canal in a way that depends on the direction and elevation of the sound source (Pickles, 2008). The waves reflecting off the ridges of the pinna and the concha will travel further than those entering the meatus directly. If the direct and reflected waves are out of phase, meaning the peak of pressure of one wave and the trough of pressure of the other arrive at the same time,

the waves will experience partial cancellation. This results in a reduction of the stimulus to the ear producing a drop in gain at approximately 10,000 Hz (Pickles, 2008). The size of the outer ear also plays an important role in sound localization. Due to the external ear being smaller in size below the meatus and larger above, Pickles (2008) suggests that the sounds reflected from the lower rim (coming from above the meatus) will arrive at the ear canal with a smaller delay than those reflected from the upper rim of the external ear. The resulting effect is that as the sound source is raised in space, the trough of the response will move toward higher frequencies.

The pinna also has passive effects on sound arriving from behind. As the sound source reaches the back of the pinna it is reflected off the edges. The resulting effect is that the direct wave is interfered with and the response is reduced in the 3,000 – 6,000 Hz region (Pickles, 2008). This is the frequency region with the greatest effects when a sound source is moved in the horizontal plane. The final fullness of sound is because of the complex shape of the pinna that provides multiple reflections that are sensitive to changes in azimuth and elevation of the sound source. The pinna, however, only contributes a small amount compared to the external auditory meatus of the overall gain of the outer ear.

**Pressure gain of the outer ear.** Together, the pinna and the external auditory meatus increase the pressure at the TM by collecting sound waves over the large area of the pinna and funneling them into the narrower canal of the meatus. As a result of the increase of pressure in the ear canal, the energy transfer to the middle ear is increased. Typically, in adult humans, the increase of pressure is a maximum of 15 - 20 decibels (dB) with a broad peak at about 2,500 Hz (Pickles, 2008). This “preferential”

transmission of sound through the external meatus to the TM at 2500 Hz is referred to as the resonance of the ear canal and concha. The specific resonant frequency for an individual occurs when the canal plus concha is one-fourth of a wavelength long. The outer ear is similar to an open tube, where there is low impedance at the open end and high impedance at the closed end. The result is increased pressure at the closed end, or at the TM. When the resonant frequency is reached the efficiency of the power transfer to the middle ear is enhanced. Both the pinna and ear canal boost the signal through resonance, with the biggest gain seen between 1,500 Hz and 8,000 Hz (Seikel et al., 2005). The total contribution of the outer ear system can result in a net gain reaching 20 dB at approximately 2,700 Hz.

### **Middle Ear**

The primary structures of the middle ear include the TM, three ossicles, and the entry to the cochlea or the oval window. The bones in the middle ear are the malleus, shaped like a club and embedded in the TM; the incus, cone-shaped and articulating with the head of the malleus in a comparatively rigid manner; and the stapes, consisting of an arch and footplate with the former attached to the incus and the latter resting on the oval window (Goelzer, Hansen, & Sehrndt, 2001). These ossicles are connected to the walls of the middle ear space by a series of ligaments. There are six ligaments in the tympanic cavity – three connecting the malleus to the tympanic cavity wall (anterior, superior, and lateral), two connecting the incus (superior and posterior), and one attaching the stapes to the middle ear wall (Gentil et al., 2013). The ligaments offer support throughout the ossicular chain, with the most stress placed on the superior malleal ligament.



**Area ratio.** The middle ear, much like the outer ear, is designed to increase pressure of the incoming signal. Specifically, the middle ear has to overcome the resistance to the flow of energy and increase the pressure arriving at the cochlea. Its primary goal is to match the impedance of the auditory meatus to the much higher impedance of the cochlear fluids in the inner ear. The large difference in the impedance of the air of the middle ear and fluid of the cochlea could potentially result in 99.9% of the sound energy being reflected with only 0.1% of the energy converted into vibrations of the fluid (Møller, 1994). This impedance mismatch is overcome by the simple principle of pressure being the ratio of force to the area over which that force is distributed. In order to increase the pressure arriving at the oval window, either the force must be increased or the area must be decreased. The middle ear transform is a result primarily of the latter, thus matching the impedance of the outer ear to the cochlear fluid in the inner ear. This first mechanism is the result of the area difference between the TM, which has an area of 55 millimeters squared ( $\text{mm}^2$ ), and the oval window, with an area of  $3.2 \text{ mm}^2$  in the adult ear (Seikel et al., 2005). This is equivalent to the TM being 17 times larger than the oval window, thus increasing the pressure at the entrance to the inner ear. Funneling of the signal from the much larger TM to the much smaller oval window results in a gain of 17:1 and an increase of 25 dB (Seikel et al., 2005).

**Lever action of the ossicles.** The second important mechanism involved with the impedance transformer of the middle ear is the lever action of the ossicles. This is a comparatively small portion of the overall impedance match; however, it does contribute an increase in the impedance ratio by approximately 4.4 times (Pickles, 2008). The

additional increase in force is contributed to the anatomy of the middle ear. The arm of the incus is shorter than the malleus and, consequently, produces a lever action of the ossicles. According to Pickles (2008), the malleus is about 2.1 times the length of the incus resulting in an increase in force of approximately 2.1 times. Furthermore, the velocity of the ossicles in the middle ear is decreased 2.1 times. The outcome of an increase in force and decrease in velocity is an overall increase in the impedance ratio of 4.4 times (pressure/ velocity ratio equal to  $2.1^2$ ), resulting in an increase of 2 dB (Pickles, 2008; Seikel et al., 2005).

The impedance matching of the middle ear is not perfect. Its greatest performance occurs around 1,000 Hz with a band-pass characteristic. In human temporal bone ears it has been found that the sound pressure at 1,000 Hz is 24.5 dB greater in the cochlear vestibule than in the ear canal measured at the TM (Aibara et al., 2001).

**Middle ear muscles.** The two smallest muscles in the body are located in the middle ear and are connected to the ossicles. These two small striated muscles can control transmission through the middle ear (Pickles, 2008). The stapedius muscle is about 7 mm (millimeters) long with a cross section of  $5 \text{ mm}^2$  and originates in the bone of the posterior wall of the adult middle ear (Martin & Clark, 2006). From there it courses through a canal located beside the facial canal and attaches to the posterior portion of the neck of the stapes. When this muscle is contracted, the stapes is rotated posteriorly and the oval window tenses. This results in a reduction in the amplitude of vibration and has been termed the acoustic reflex. The stapedius branch of the facial (seventh) cranial nerve innervates the stapedius muscle. The second middle ear

muscles, the tensor tympani muscle, is approximately 25 mm in length in the adult ear with a cross section of 5 mm<sup>2</sup> and originates from the anterior wall of the middle ear superior to the opening of the Eustachian tube (Seikel et al., 2005). It terminates with insertion into the manubrium of the malleus and is innervated by the trigeminal (fifth) cranial nerve. Upon contraction of the tensor tympani muscle, the malleus is pulled antero-medially resulting in tension on the TM and, consequently, a reduction in the movement of the TM (Martin & Clark, 2006; Seikel et al., 2005).

Activation of the middle ear muscle (MEM) reflex pathway occurs bilaterally following loud acoustic stimulation to either ear. As will be discussed later, the stapedius reflex can be tested clinically by use of the acoustic reflex test and is valuable as it can provide information regarding the function of the auditory nerve, cochlear nucleus (CN), and part of the facial nerve (Møller, 1994). Several functions have been suggested for MEMs including inner ear protection from noise damage, ability to keep intense low-frequency stimuli near a lower part of the intensity range, a beneficial effect on the frequency response of the middle ear, and a reduction in the masking effect of low frequency noise (Pickles, 2008). However, this notion has been challenged (Aiken et al., 2013; Phillips, Stuart, & Carpenter, 2002). Aiken et al. (2013) examined speech recognition scores in nine control subjects and six patients with transected stapedius tendons poststapedotomy. This study found that the stapedius reflex does offer some protection in the upward spread of masking of speech at moderate levels but not at high levels. Similarly, Phillips et al. (2002) investigated the role of the acoustic reflex by examining performance-intensity functions in 10 normal participants and six that had undergone stapedectomies. None of the patients in this study exhibited rollover in their

performance-intensity functions suggesting that if the stapedius reflex does play a role in protection from the upward spread of masking it is inconsequential for word recognition in quiet.

Contraction of the MEMs increases middle ear impedance by increasing the stiffness of the middle ear, thus reducing the transmission of sounds of low frequencies (Pickles, 2008). According to Lee et al. (2006), this supports the notion that the MEM reflexes preserve speech frequencies, which are higher frequencies, from masking by background noise, which are most often lower frequencies. Phillips et al. (2002) suggested, however, that the stapedius reflex plays an inconsequential role in protection from this idea of an upward spread of masking. In this study word recognition in quiet was examined in both normal hearing subjects with low-frequency enhanced speech and in subjects with stapedectomies. It was found that neither group of subjects exhibited any rollover in speech performance. This suggests that the stapedius reflex does not play a role in word recognition in quiet.

The MEM reflexes are primarily thought to protect the ear from intense sounds more than 75 dB above the absolute threshold and can also be activated by vocalization, tactile stimulation of the head, or general body movement, as well as in some humans without any other discernible movements (Hilding, 1960; Karlovich et al., 1977; Kobrak, Lindsay, & Perlman, 1941; Lee et al., 2006; Mills & Lilly, 1971; Pickles, 2008; Simmons, 1960; Takahashi, 1954; Zakrisson, 1975; Zakrisson, 1979). In some mammals both MEM reflexes respond to sound; however, in humans the stapedius muscle is the dominant sound evoked reflex. The general function of the tensor tympani reflex is still not well understood in humans. Previous researchers have

suggested that it is activated by intense sounds as part of a startle reflex as well as by certain nonauditory stimuli including tactile stimulation of the external auditory canal and face, pneumatic pressure on the eyelids, and swallowing (Mukerji, Windsor, & Lee, 2010).

Either ear can elicit the MEM reflex with a response to the stimulation by both ears. The ipsilateral reflex pathway to the stimulated ear elicits larger responses than the reflex pathway contralateral to the side of stimulation. The ipsilateral stapedius reflex pathway is as follows: outer ear → middle ear → inner ear → auditory nerve → CN in the brainstem → superior olivary complex (SOC) → facial nerve → stapedius muscle of the ipsilateral middle ear. Almost simultaneously neural impulses cross the brainstem to the opposite SOC, which then sends the information via the facial nerve to the stapedius muscle on the opposite side of stimulation, resulting in the contralateral reflex pathway. As such, the contralateral pathway is: outer ear → middle ear → inner ear → auditory nerve → CN in the brainstem → SOC contralateral to stimulation → facial nerve contralateral to stimulation → stapedius muscle of the contralateral ear.

A number of theories as to the role of the acoustic reflex have been proposed. The intensity control-protection theory was introduced as early as the beginning of the seventeenth century and suggests that intensity control is exerted by the stapedius muscle at relatively moderate sound levels and, at considerably higher sound levels, the tensor tympani becomes reflexively active (Borg, Counter, & Rösler, 1984). According to Borg et al. (1984), the ossicular-chain fixation theory proposes that the tensor tympani and stapedius muscles serve primarily to maintain the position of the ossicular structures in a state of readiness for effective sound transmission. Recent evidence has

shown that severing the middle ear muscles or tendons renders the ossicular chain more fragile. The accommodation-frequency selection theory suggests that the ear gives selective transmission of certain sounds as a result of the contraction of the middle ear muscles. This notion was challenged by Brücke in 1884. He suggested that the reaction of middle ear muscles is too slow to respond rapidly to changing sounds and different kinds of noise (Borg et al., 1984). According to Borg et al. (1984), it has also been theorized that the contraction of the middle ear muscles “causes an increase in the pressure of the labyrinthine fluids and thereby damps the effect of the acoustic energy reaching the inner ear (p. 71). This is known as the labyrinthine pressure-regulation theory and research has shown that these labyrinthine pressure changes noted during contraction of the middle ear muscles do not have an effect on the hearing process.

In addition to the above mentioned theories of the role of the acoustic reflex there have been other hypotheses and observations on the topic. It has been suggested that the tensor tympani muscle results in a subjective softening of low-pitch tones. The result is that higher-pitch tones are clearer and hearing for faint high tones is improved (Borg et al., 1984). Additionally, the stapedius muscle has been suggested to improve hearing of low frequency tones and, ultimately, improve hearing of all faint sounds. It has also been reported that the middle ear muscles enhance certain aspects of sound localization and improve auditory perception. According to Borg et al. (1984), some researchers have also suggested that the middle ear muscles primarily serve to induce noise in the hearing system with the tensor tympani producing high-pitch noise and the stapedius muscle generating low-pitch noise. Finally, there have been some

researchers to suggest that these muscles serve no active function at all and are considered rudimentary in nature.

## **Inner Ear**

The inner ear is responsible for interpreting information regarding hearing as well as information regarding the body's position and movement. The vestibular system relies on the forces of gravity and inertia, interpreting both linear and angular acceleration, and will not be the focus of this work. The outer and middle ears amplify the incoming signal by approximately 30 dB (Goelzer et al., 2001). The task from this point forward is for the vibration to be transduced into a neural impulse and sent up the auditory pathway to the auditory cortex. The cochlea of the inner ear is responsible for processing the acoustic signals of speech including spectral and temporal information (Seikel et al., 2005).

The cochlea is a fluid-filled duct located within the temporal bone on either side of the head and in humans stands about 10 mm wide and 5 mm from base to apex with an uncoiled basilar membrane length of approximately 34 mm (Ashmore, 2008; Pickles, 2008). The cochlea is divided longitudinally into three scalae, which spiral together the length of the cochlea and include the scala vestibuli, scala media, and scala tympani. These will be discussed in detail below.

**Organ of Corti.** The true end organ of hearing is the organ of Corti, located on the basilar membrane. The basilar membrane is one of the three walls of the scala media, separating the scala media from the inferior scala tympani. The other two walls include Reissner's membrane, separating the scala media from the superior scala vestibuli, and a bony shelf formed by a portion of the bony labyrinth (Martin & Clark,

2006). The basilar membrane varies in width from less than 0.1 mm at the basal turn to about 0.5 mm at the apical turn and reacts to vibrations of the inner ear more than any other structure (Martin & Clark, 2006). It is comprised of numerous taut, parallel fibers that are resonant at progressively lower frequencies travelling from the base to apex of the cochlea (Goelzer et al., 2001).

The organ of Corti is where the sensory hair cells (HC) are located, as well as the nerve endings and supporting cells. Medially, there is one row of inner hair cells (IHCs) closest to the central core of the cochlea. IHCs are innervated primarily by afferent nerve fibers and account for approximately 3,000 HCs in humans (Møller, 1994). Three to four rows of about 12,000 outer hair cells (OHCs) have a much less pronounced afferent innervation, accounting for only about five percent of afferent nerve fiber innervation (Ashmore, 2008; Møller, 1994). The function of the supporting cells in the organ of Corti is to maintain potassium (K<sup>+</sup>) in the scala media.

Above the organ of Corti is the tectorial membrane, a gelatinous and fibrous flap where the longer of the hairs, or stereocilia, on the OHCs are firmly embedded on the underside (Pickles, 2008). The tectorial membrane is raised above the basilar membrane and is only attached on its inner edge. Consequently, when the basilar membrane moves up and down in response to fluid displacement in the inner ear as a result of the in and out movement of the stapes, the tectorial membrane also moves in a shearing manner. This results in the deflection of stereocilia located on the apical surface of the HCs.

**Travelling wave.** Incoming sound arrives at the TM and vibrates the middle ear ossicles transmitting the signal to the inner ear from the oval window. These vibrations



cause movement of the fluid within the cochlea, ultimately ending at the round window. The oval and round windows serve as a pressure equalizing mechanism for the cochlear fluid, which will be discussed in detail below (Goelzer et al., 2001). The travelling wave is a result of deflection of the basilar membrane due to the sound-displaced cochlear fluids (Pickles, 2008). The movement of cochlear fluids in conjunction with the stiffness of the basilar membrane causes a progressive travelling wave of energy on the membrane that passes from the base to apex of the cochlea.

The travelling waves differ depending on the frequency of the incoming signal. Sounds of higher frequency will result in a travelling wave that peaks nearest to the oval window at the base of the cochlea, consequently resulting in the transduction of high-frequency sounds near the base of the cochlea. Low-frequency sounds, on the other hand, are transduced near the apex of the cochlea.

The cochlea is a “remarkably efficient frequency analyser” (Goelzer et al., 2001, p. 58). The travelling wave is sharply tuned due to the active mechanical response of the OHCs that amplifies the vibration of the basilar membrane as the travelling wave passes along the cochlear duct (Pickles, 2008). This results in an increase in the travelling wave amplitude until the wave ceases at a point on the basilar membrane where it can no longer sustain vibrations of that particular frequency. The largest effect of this active amplification is seen at low stimulus intensities with a smaller contribution occurring at higher intensities. It can be said that the basilar membrane moves with compressive nonlinearity, meaning that the response does not grow as fast as the input (Pickles, 2008). This allows the auditory system to interpret sounds across a vast array of intensities.

**Fluid spaces.** The sharply tuned travelling wave of the inner ear is due, in part, to the electrochemical environment of the cochlea. The cochlear scalae are divided into endolymphatic and perilymphatic spaces, which differentiate from one another by the chemical makeup of their respective fluids. Endolymph can be found in the scala media and contains a high level of  $K^+$  and a low level of sodium ( $Na^+$ ), much like the fluid found inside resting muscle cells (Pickles, 2008). This inner endolymphatic space is bounded above by Reissner's membrane, laterally by the stria vascularis, and below by the upper surface of the organ of Corti (Pickles, 2008). The boundaries of the endolymphatic space are made up of occluding tight junctions, which are known to inhibit ionic movement. The endocochlear direct current (DC) potential, or the potential within the scala media, is a strong positive resting potential averaging about 80 millivolts (mV) due to the high  $K^+$  concentration (Martin & Clark, 2006). The positive potential in the endolymphatic space increases the flow of  $K^+$  out of this space through mechanotransducer channels in the HCs. At this point the  $K^+$  is then recycled through the stria vascularis, which is the major blood supply to the cochlea and is responsible for maintaining the unique concentration of  $K^+$  in the endolymph and the endocochlear potential.

The perilymph is contained in the scala vestibuli as well as in the scala tympani and is similar to that of extracellular fluid or cerebrospinal fluid, with the chemical makeup of this fluid having a concentration of 140 – 150 millimolar (mM) of  $Na^+$  and only 4 – 6 mM of  $K^+$ . The electric potential of perilymph differs slightly between the scala tympani and scala vestibuli. The resting potential of the scala vestibuli is slightly more positive (i.e., about 5 mV) than the resting potential of the scala tympani (Seikel et

al., 2005). The remaining cochlear structures exhibit a negative DC resting potential (Martin & Clark, 2006).

**Hair cells.** The role of the HCs in the inner ear is to signal movement of the cochlear partition to the central nervous system by amplifying the mechanical travelling wave (Pickles, 2008). HCs are located between the basilar membrane and a thin sheet of tissue called the reticular lamina. On the apical portion of the HCs are mechanosensing organelles, or stereocilia. The stereocilia extend above the reticular lamina and into the endolymph (Bear, Connors, & Paradiso, 2007).

IHCs and OHCs can be differentiated by several means. As previously discussed, there is one row of IHCs innervated primarily by afferent nerve fibers and three to four rows of OHCs, which receive primarily efferent nerve fibers. HCs have an intracellular fluid high in  $K^+$  and low in  $Na^+$  with a resting potential of approximately -45 mV and -70 mV for IHCs and OHCs, respectively. IHCs are flask-shaped and are completely surrounded by supporting cells in the organ of Corti (Musiek & Baran, 2007). The stereocilia of the IHCs are arranged linearly and are not embedded in the tectorial membrane, but end just below the tectorial membrane. The primary function of the IHCs is sensory transduction, which will be discussed in detail below. OHCs, on the other hand, specifically contribute to amplification of the basilar membrane motion. They are cylindrically shaped with each base resting in the cup of a Deiter's cell and the stereocilia are arranged in a "W" shaped pattern (Musiek & Baran, 2007). The stereocilia on the OHCs are embedded in the tectorial membrane.

The basilar membrane, reticular lamina, and HCs are rigidly connected, moving as one unit in response to sound. As a result of the stereocilia of the OHCs being

embedded in the tectorial membrane, the lateral motion of the reticular lamina bends the stereocilia of these cells in one direction or the other (Bear et al., 2007). The IHCs also bend in response to this motion; however, this is most likely do to the fact that they are pushed by the moving endolymph.

**Transduction.** The endolymphatic potential and intercellular fluid voltage difference is critical for sensory transduction. Sensory transduction involves basilar membrane motion, activation of mechanically sensitive channels, diffusion of ions down an electrochemical gradient, change in HC membrane voltage, activation of voltage gated ion channels, and the release of the neurotransmitter.

According to Ashmore (2008), “hair cells are neuroepithelial cells, with the apical pole specialized for mechanotransduction and the basal pole specialized for the release of neurotransmitter” (p. 174). Tight junctions join the apical circumference of HCs to the surrounding supporting cells preventing any mixing of endolymph and perilymph (Santos-Sacchi, 2001). The stereocilia are arranged in bundles and, as the basilar membrane moves up and down during each cycle induced by sound, deflect towards the tallest stereocilia row. This results in a depolarization of the cell from its negative resting potential which, in turn, results in an increase of neurotransmitter release and excitation of the nerve fiber. When the stereocilia bundles are deflected in the opposite direction hyperpolarization occurs, with a decrease in neurotransmitter release and inhibition of fiber activity.

The depolarization following deflection of stereocilia towards the tallest stereocilia row is dependent on the “specialized structural attachments at the tops of stereocilia” (Santos-Sacchi, 2001, p. 363). These structures are called tip links and are elastic

filaments located at the tips of the shorter stereocilia and join to the side of the adjacent taller stereocilium. This provides the tension required to open the transduction channels during deflection. If the tip links are broken, the mechanically gated channels will not function. Once these channels open, there is an influx of  $K^+$  through the open channels and into the HC. This is the result of the voltage difference between the positive endocochlear potential and the negative HC intracellular potential, causing the  $K^+$  to diffuse down a huge electrical gradient (Pickles, 2008). As the  $K^+$  diffuses into the HC, the intracellular potential becomes more positive and depolarization occurs. As depolarization occurs, voltage gated calcium ( $Ca^{2+}$ ) channels located on the basolateral membrane of the HC open and  $Ca^{2+}$  enters the HC (Bear et al., 2007; Santos-Sacchi, 2001). The  $Ca^{2+}$  influx mobilizes synaptic vesicles as well as leads to the activation of  $Ca^{2+}$ -activated  $K^+$  channels allowing the outward flow of  $K^+$ . This increased intracellular  $Ca^{2+}$  in the HC promotes the release of neurotransmitters, in this case glutamate, from the bottom of the HC. Glutamate, once released, diffuses across the synaptic cleft, binds to the receptors on the postsynaptic membrane of the afferent nerve fiber, and depolarizes the fibers enough to generate an AP (Musiek & Baran, 2007). The AP is then transmitted as nerve impulses via the auditory nerve up to the auditory cortex of the brain.

The stria vascularis plays a critical role in the maintenance of the endocochlear potential (Musiek & Baran, 2007). It is the major blood supply to the cochlea and is also responsible for maintaining the unique concentration of  $K^+$  in the endolymph and the endocochlear potential. According to Wangemann (2002), the “stria vascularis in the lateral wall of the cochlea is a multi-layered, highly vascularized epithelium that is part of

the epithelial barrier enclosing endolymph” (p. 3). This endocochlear potential is maintained with the use of several different ion transport mechanisms within the inner ear.  $K^+$  is recycled from the endolymph through the HCs, the fibrocytes in the spiral ligament, the stria vascularis, and back to the endolymph (Musiek & Baran, 2007).

According to Steel and Barkway (1989), the stria vascularis is made up primarily of three types of cells: basal cells, intermediate cells, and marginal cells. Basal cells have an elongated shape and are located next to the spiral ligament in the stria vascularis. These cells are connected by tight junctions, which are responsible for forming the continuous barrier between intrastrial fluid and the spiral ligament contained in the cochlear wall (Carlisle, Steel, Forge, 1990). Intermediate cells, on the other hand, are dispersed throughout the stria vascularis. They are often located near capillaries and are sandwiched between marginal cells and basal cells.

Marginal cells form a continuous barrier between the fluid within the stria vascularis and the endolymph. These cells are located on the endolymphatic surface of the stria vascularis and have a complex shape. They are thought to be directly involved with the active ion transport of  $K^+$  in the inner ear and have membranes rich in  $Na^+/2Cl^-/K^+$  cotransporters and  $Na^+$ ,  $K^+$  - ATPase, indicating high metabolic activity (Pickles, 2008). These pumps are responsible for moving  $K^+$  out of the intrastrial space resulting in a low concentration of  $K^+$  in the intrastrial fluid. There are also  $K^+$  channels on the apical side of the marginal cells where  $K^+$  can diffuse down its concentration gradient, moving from the stria vascularis into the endolymph. Marginal cells are unique in that they contain a high intracellular resting potential of about +90mV

that has suggested a role in producing the special endocochlear potential (Carlisle, Steel, Forge, 1990).

There have been four ion transport mechanisms identified for maintaining the high  $K^+$  concentration in the endolymph (Musiek & Baran, 2007). The first mechanism is located on the apical membrane of the marginal cells in the stria vascularis and is a selective  $K^+$  channel, which releases  $K^+$  into the endolymph. The membrane potential across the apical surface of the marginal cells is only about 0 to +10 mV, allowing for slow diffusion of  $K^+$  down this small electrochemical gradient. The second transport mechanism is located on the basolateral membrane of the marginal cells. This  $Na^+/K^+$ -ATPase pump takes up two  $K^+$  ions while three  $Na^+$  ions are extruded into the intrastrial space. The third mechanism involves the  $Na^+/2Cl^-/K^+$  cotransporter. It contributes to the uptake of three additional  $K^+$  ions, as well as  $Na^+$  and  $Cl^-$  from the intrastrial space (Musiek & Baran, 2007). The last of the four ion transport mechanisms is a  $Cl^-$  channel, also located on the basolateral wall of the marginal cells. This channel contributes to the flow of  $Cl^-$  into the intrastrial space. The combined result of the four ion transport mechanisms is a low concentration of  $K^+$  in the intrastrial space with a high concentration of  $K^+$  in the intermediate cells. This leads to the large potential difference between the intrastrial fluid and the cytosol of the intermediate cells, which is thought to be responsible for the endocochlear potential (Musiek & Baran, 2007).

**Gross evoked cochlear potentials.** Electrodes located in or near both animal and human cochlea have recorded gross evoked potentials produced by the large number of nerve cells (Pickles, 2008). These responses have contributed to much of our current understanding of cochlear function. One evoked potential recorded from the

cochlea is the endocochlear potential, as previously discussed. According to Musiek and Baran (2007), the voltage gradients in fluid-filled compartments, like the endocochlear potential, can be measured by passing an electrode from the scala tympani through the organ of Corti and into the scala media. When an acoustic stimulus is presented to the cochlea, sound-evoked cochlear potentials can also be recorded due to the change in the electrical current flowing through HCs. There are two sound-evoked cochlear potentials: the cochlear microphonic (CM) and the summing potential (SP). These potentials can be recorded in either the fluid filled spaces of the cochlea or at locations near the generator, such as the round window, the promontory, the surface of the TM, or the ear canal (Musiek & Baran, 2007).

Wever and Bray (1930) were the first to demonstrate the notion that acoustic signals could be transduced into electrical signals, establishing a definite correlation between the frequency of the acoustic stimulation and the frequency of impulse in the auditory nerve. Wever and Bray, however, thought that the origin of the CM was from the auditory nerve and not the OHCs (Guinan, Salt, & Cheatham, 2012). The first in vivo intracellular HC recordings were in the guinea pig cochlea and were recorded from IHCs at the base of the cochlea (Russell & Sellick, 1978). These were later supplemented by IHC and OHC recordings from the apex of the cochlea by Dallos et al. (1982). According to Guinan et al. (2012), Georg von Békésy's experimental work using a vibrating electrode demonstrated that "the CM was proportional to BM displacement not velocity" (p. 13) and foreshadowed the intracellular work showing that OHCs respond to basilar membrane displacement.



The CM is an alternating current (AC) voltage whose frequency response mimics the acoustic stimulating waveform (Pickles, 2008). The CM occurs with essentially no time delay between the eliciting stimulus and the CM response and is the earliest and smallest electrical response recorded from the normal human auditory system (Musiek & Baran, 2007). It is a direct reflection of the displacement along the basilar membrane in the cochlea in response to sound. This response is derived mainly from the currents that flow through the OHCs in the basal portion of the cochlea and may be best visualized when elicited with a low to medium frequency tone (Møller, 1994; Pickles, 2008). The CM follows the polarity of the eliciting stimulus and, as a result, can be cancelled by averaging the response to a stimulus of alternating polarity (Hall, 2007). This cancellation technique aids in visualization of the SP and AP responses.

The SP is a complex response containing several components. The SP gets its name due to the fact that it is a summation of sound-evoked potentials (Møller, 1994). It is similar to the CM in that it is a stimulus-dependent response generated by the HCs in the organ of Corti. It is also a direct reflection of the displacement-time pattern of the cochlear partition and is primarily generated by the IHCs (Ferraro & Durrant, 2006; Hall, 2007). The SP response follows the envelope of the eliciting stimulus and appears as a deflection of the baseline. It does not appear to mimic the eliciting stimulus like the CM, but has a DC voltage instead. The SP, according to Hall (2007), is not markedly influenced by stimulus frequency, however, is directly affected by stimulus duration. The role of the SP is not completely understood. According to Ferraro and Durrant (2006), "its components are thought to represent nonlinearities associated with the transduction processes in the cochlea" (p. 47). The SP is useful for monitoring cochlear

pathology and clinical conditions including Ménière's disease (MD).

### **Anatomy and Physiology of the Human Central Auditory System**

The conduction of sound up to the auditory nerve has been discussed at this point. From here, this neural activity must travel the auditory nerve to be processed by the central auditory system. The connections in the central auditory pathway are very complex, with numerous crossed and uncrossed pathways and reflexes. A brief discussion on the structures and functions of the central auditory pathway will follow.

#### **Auditory Nerve**

The AP is a far field representation of the compound AP of the eighth cranial nerve, or the auditory nerve (Hall, 2007). It is the same as wave I of the auditory brainstem response (ABR), however, is often recorded with negative polarity for electrocochleography (ECochG) due to the horizontal electrode montage utilized during recording, which places the noninverting electrode at the test ear. The AP response reflects the synchronous firing of several thousand auditory nerve fibers and occurs at the onset of the stimulus (Ferraro, 2000). This response arises from the distal portion of the auditory nerve and is thought to be a reflection of IHC output, as the majority of the afferent auditory nerve fibers innervate the IHCs and is independent of stimulus phase and duration. The AP is a graded potential that increases in amplitude with increasing stimulus intensity (Musiek & Baran, 2007). The threshold of the AP is the lowest stimulus level at which an AP can still be visualized. The AP threshold is documented to be between 10 and 20 dB above the behavioral thresholds in animals (Dallos, 1975) and humans (Eggermont & Odenthal, 1974) allowing for it to be used as a valuable clinical tool to estimate hearing threshold changes due to cochlear damage. The useful

features of the AP include its latency and amplitude measures, with the latter being a reflection of the number of nerve fibers firing (Ferraro, 2000). The utility of AP measures in noise-exposed subjects will be discussed in detail below.

## **Brainstem**

Several of the initial central structures in the auditory system are located in the brainstem rostral to the 8<sup>th</sup> nerve. Moving caudal to rostral, these structures include the CN, SOC, lateral lemniscus (LL) in the pons, inferior colliculus (IC) in the midbrain, and the medial geniculate body (MGB) in the thalamus (Musiek & Baran, 1986a). There are some additional structures posterior to and in the brainstem that have been discovered to play a role in auditory function. The reticular formation is a medial structure located within the brainstem that has many direct and indirect inputs from other various auditory nuclei. This structure appears to play a major role in auditory alertness, reflexes, and habituation (Musiek & Baran, 1986a). According to Mukerji et al. (2010), the reticular formation controls behavior and arousal states through the release of serotonin.

**Cochlear nucleus.** The CN is the most caudal structure of the central auditory pathway, receiving direct innervation from the auditory nerve and serving as the first relay station for all ascending auditory information (Mukerji et al., 2010). This structure is the first in the central auditory pathway where actual processing of the auditory signal occurs (Bellis, 2003). There are three divisions of the CN: the anterior ventral, posterior ventral, and dorsal CN. All three of the CN divisions are tonotopically arranged and each responds to its own range of characteristic frequencies. The CN tuning curves are wider than those of the auditory nerve, suggesting that the CN preserves frequency resolution but does not enhance it (Musiek & Baran, 1986). The auditory nerve has

three branches with each branch innervating a different division of the CN. CN interneurons found in the ventral CN contribute to the MEM reflex.

Research studies have examined the role of the CN in auditory function by placing recording electrodes in the vicinity of the CN in humans. This structure is located deep within the brainstem on the posterolateral surface of the ponto-medullary junction under the cerebellar peduncle and is consequently rarely exposed during neurosurgical operations (Møller & Jannetta, 1983). As a result of the anatomical position of the pons, medulla, and cerebellum a lateral recess is formed. Successful electrophysiological recordings from the CN have been obtained, however, by placing electrodes in this recess, or cerebello-pontine angle (CPA), during operations for cranial nerve dysfunction. The results from these recordings point to the ipsilateral CN as the main generator of wave III of the ABR in man (Møller & Jannetta, 1983). Tumors can develop in the CPA, ultimately affecting the CN with resulting central auditory deficits (Musiek & Baran, 1986).

The primary function of the CN is enhancement of certain features of the neural signal, including contrast enhancement (Bellis, 2003). All three divisions of the CN are tonotopically arranged and CN neurons show evidence of inhibitory influences, which contribute to the narrowing of tuning in the CN fibers. As a result, the CN fibers have increased frequency selectivity and their temporal and spectral response properties affect the representation of complex signals such as speech (Musiek & Baran, 2007). The CN also plays an important role in sound localization.

Once the acoustic signal has been processed in the CN, it can take three primary routes up the auditory pathway: the dorsal CN along the dorsal acoustic stria to the LL,

the anterior ventral CN along the ventral acoustic stria to the SOC and LL, and the posterior ventral CN along the intermediate acoustic stria to the SOC and LL. These pathways are primarily contralateral pathways, with some fibers traveling ipsilaterally to various brainstem nuclei (Musiek & Baran, 2007).

**Superior olivary complex.** The SOC is the next anatomical structure in the central auditory pathway and is located medially and ventrally to the CN (Musiek & Baran, 1986). This structure is composed of five main nuclei groups: the lateral superior olivary nucleus, the medial superior olivary nucleus, the trapezoid body, the medial preolivary nucleus, and the lateral preolivary nucleus. The SOC receives bilateral innervation from both the ipsilateral and contralateral CN and is responsible for processing binaural input. Processing in the SOC allows for sound localization, lateralization, and binaural integration (Bellis, 2003).

The SOC is responsible for decoding the binaural cues as they arrive from the CN. It does this in two primary ways. According to Bellis (2003), “the medial superior olive of the SOC is innervated by successive branches of incoming neurons from both the ipsilateral and contralateral CN” (p. 26). This pattern of innervation allows for an interaural time delay as a result of the divergence of input from one neuron to numerous cells in succession. There are also branches of some ascending CN fibers from both ears that arrive at a single SOC cell at different times as well as a number of cells within the SOC that respond preferentially to specific timing differences between the ears (Bellis, 2003). This arrangement of input from the CN provides the auditory cortex with information regarding localization of a sound source by utilizing both interaural time and phase differences.

In addition to the innervation of cells in the SOC contributing to the binaural coding of information in the auditory system, the excitation and inhibition patterns also play an important role. According to Bellis (2003), this is accomplished due to the signal from the ipsilateral ear arriving at the lateral superior olive directly from the CN while information from the contralateral ear passes first through the medial nucleus of the trapezoid body. The trapezoid body appears to serve an inhibitory function with the result being excitatory input from the ipsilateral ear with inhibitory input from the contralateral ear. Consequently, the inputs cancel one another out and there is no response from these SOC cells. This becomes important when there is unilateral stimulation or an intensity difference between the two ears. The pattern of excitatory and inhibitory responses enhances the cues that are important for localization of auditory stimuli (Bellis, 2003). The functions of the SOC contribute to binaural hearing and can specifically aid in speech-in-noise skills.

**Lateral lemniscus.** In general, there has been a paucity of research and interest in the physiological function of the LL. It is accepted, however, that the neural fibers that run through the LL represent the major auditory pathway that associates the pons and the midbrain, the LL is composed of ascending and descending fibers, and is considered to be the primary ascending auditory pathway (Musiek & Baran, 2007; Bellis, 2003). The LL has two nuclei groups, termed the ventral nucleus and the dorsal nucleus. The pathway to each is comprised of fibers from the contralateral CN and the ipsilateral SOC. Anatomically, the LL is located in the lateral portion of the pons, which makes it vulnerable to extrinsic lesions originating from the auditory, facial, and trigeminal cranial nerves (Musiek & Baran, 2007). The ventral nucleus is located more

caudal and is a more elongated structure than the dorsal nucleus, which is located immediately caudal to the most caudal aspect of the IC. The commissure of Probst functionally connects the LL on both sides of the brainstem.

According to Musiek and Baran (1986), most of the neurons in the ventral nucleus are activated only by contralateral stimulation while most of the neurons in the dorsal nucleus are activated by binaural stimulation. There is definite tonotopic organization in the LL, with the low frequencies located in the dorsal region and the high frequencies located in the ventral region in both the dorsal nucleus of the LL and ventral nucleus of the LL. It is now suggested that the tonotopicity is not as organized in the ventral nucleus as in lower auditory nuclei or even the dorsal nucleus of the LL (Musiek & Baran, 2007). The tonotopic organization of the ventral nucleus has more recently been described to resemble a corkscrew, or “helicoid” organization (Merchán & Berbel, 1996).

The ventral nucleus of the LL has a precise phase-locking ability and is sensitive to interaural time differences. This seems to play a role in temporal processing either at this level or for transmission to higher levels of the auditory system for processing. The ventral nucleus also has cells that are responsive to only ipsilateral stimulation, others that respond to just contralateral stimulation, and some that respond to binaural stimulation. The dorsal nucleus has a large number of cells responsive to binaural input and interaural intensity differences (Musiek & Baran, 2007). Much like the SOC, the LL contributes to localization cues. According to Musiek and Baran (2007), the neural activity of the LL is the primary contributor to wave V of the ABR with lesser contributions from the IC.

**Inferior colliculus.** The IC is located on the dorsal portion of the midbrain and is easily viewed by removing the cerebellum. This structure is recognized as two spherical mounds resembling pearls located on the posterior surface of the brainstem. Immediately caudal to the IC is the superior colliculus, which is essential for the sense of vision. Both inferior colliculi are connected by commissural fibers called the brachium and, as a result, play an important role in the localization of sound sources and other binaural processes (Bellis, 2003).

There are three main divisions of the IC: the central nucleus, the dorsal cortex, and the external (or lateral) nucleus. According to Musiek and Baran (1986), the central nucleus, or “core”, is composed of purely auditory fibers (p. 214). The dorsal and external regions, on the other hand, have some somatosensory representation and are much less organized auditorily than the central nucleus (Musiek & Baran, 2007).

According to Bellis (2003), “the IC exhibits a *nucleotopic* organization in which different subdivisions receive multiple (parallel) sets of input from lower brainstem structures” (p. 28). These inputs of information arrive from the contralateral CN, SOC, dorsal nucleus of the LL, and IC, as well as the ipsilateral CN, lateral SOC, medial SOC, dorsal nucleus of the LL, and ventral nucleus of the LL. The largest single source of input to the IC is from the ventral nucleus of the LL (Musiek & Baran, 2007). The primary output tracts of the auditory signal as it passes through the IC are ipsilaterally through the brachium of the IC to the MGB. There are contralateral connections to the MGB and projections to the posterior nucleus of the thalamus.

Much like the other auditory structures discussed to this point, the IC exhibits frequency tonotopicity. The tonotopicity of the IC is organized in isofrequency strips,



meaning that each sheet of cells corresponds to a single point on the cochlear basilar membrane. In the IC the low frequencies are located dorsolaterally and the high frequencies progress in a ventrolateral direction (Musiek & Baran, 2007; Musiek & Baran, 1986). The majority of tuning curves in the IC have been noted to be extremely sharp suggesting that the IC has great frequency resolution.

The primary role of the IC is to further enhance the modulations of the acoustic signal, which aids in speech encoding. Encoding of binaural signals also occurs in the IC, as some neurons in the IC are sensitive to phase differences and some are sensitive to interaural intensity differences. It is in the IC that the auditory pathway divides into two main pathways: the primary (cochleopathic) pathway and the diffuse (noncochleopathic) pathway (Bellis, 2003). The main differences between these pathways are where they originate and the tonotopic characteristics; the cochleopathic pathway originates in the central nucleus of the IC and exhibits sharp frequency tuning with tonotopic organization and the noncochleopathic pathway originates in the pericentral nucleus and exhibits broad frequency tuning with very little tonotopicity. It is suggested that these pathways serve different functions and project to different areas in the auditory cortex (Bellis, 2003).

**Medial geniculate body.** The MGB is the auditory nucleus of the thalamus and can be easily observed by removing the temporal lobe. It is located on the dorsolateral surface of the thalamus. The thalamus can be identified as a large oval structure located rostral and lateral to the brainstem axis (Musiek & Baran, 2007). The IC and the MGB are only separated by about 1 cm even though the IC is located in the midbrain and the MGB is located in the thalamus (Musiek & Baran, 2007).

The MGB can be separated into three divisions: ventral, dorsal, and medial divisions. The ventral division of the MGB is highly auditory with its composition made up of primarily acoustically responsive cells. Different regions of the MGB often receive acoustic information from the same source, but respond in different manners. Some regions of the MGB also receive nonauditory information and project these signals to various nonauditory cortical areas, suggesting that the MGB plays a role in multimodality integration (Bellis, 2003). In addition to multimodality integration, the MGB contributes to the processing of acoustic stimuli by enhancing amplitude modulations, extracting acoustic features, encoding of binaurality, and additional complex signal processing and it has been suggested that the MGB begins the processing of natural speech stimuli (Bellis, 2003; Musiek & Baran, 1986).

### **Cerebrum**

The cerebrum is composed of four regions, or lobes: the parietal, occipital, temporal, and frontal lobes. Every region of the cerebrum encompasses neurons that are responsive to acoustic stimulation. The cerebrum also has two main auditory areas. These include the primary auditory cortex, or cochleotopic, and the auditory association cortex, or noncochleotopic. The primary auditory cortex is called Heschl's gyrus and is located on the upper surface, or supratemporal plane, of the temporal lobe and is usually found in the left hemisphere (Bellis, 2003). Heschl's gyrus can vary greatly between specimens, with some individual brains containing double gyri on each side and others having two gyri on the left and one on the right or vice versa (Musiek, 1986b).

Projections from the MGB are received in the auditory cortex via the internal capsule, insula, and external capsule and this pathway is often referred to as the thalamo-cortical pathway (Bellis, 2003; Musiek, 1986a). The insula, specifically, is located medial to the middle segment of the superior temporal gyrus and is responsive to acoustic, somatic, visual, and gustatory stimulation (Musiek, 1986a). There are four kinds of neuronal responses in the auditory cortex. The first neuronal response is for the duration of the stimulus. There are also neurons that respond only to the onset, neurons that respond only to the offset, and neurons that respond to the onset and the offset but do not respond for the duration of the stimuli (Musiek, 1986a).

The auditory cortex retains the tonotopic organization of the cochlea. There seem to be multiple tonotopically organized auditory fields in the auditory cortex with little understanding of how these multiple auditory fields effect speech perception. The tonotopicity of the middle layers of the primary auditory cortex are such that the low frequencies are represented posteriorly and the high frequencies anteriorly. Fibers in the primary auditory cortex are also organized in ear-dominance bands, allowing for patterns of response to ear specific stimulation to occur in each band regardless of frequency (Bellis, 2003).

The primary auditory cortex demonstrates an excellent ability in coding rapid acoustic events that are so important for understanding speech stimuli and is essential to the development of the concept of auditory space and the ability to localize the acoustic stimuli (Bellis, 2003). Temporal coding, or the discharging of neurons in the primary auditory cortex, is nearly as precise to the onset of the stimulus as the auditory nerve. This is important to speech perception, as this represents the phonetically

important aspects of speech such as voice onset time and place of articulation. The auditory cortex is also better prepared to respond to complex stimuli than to simple stimuli and seems to play a role in the processing of speech stimuli that are dichotically presented (Musiek, 1986a; Musiek & Baran, 2007).

The primary auditory cortex is connected via an extensive axonal bundle to the auditory association cortex, or Wernicke's area. Wernicke's area contributes to the recognition of linguistic stimuli, comprehension of spoken language, and some language formation ability (Bellis, 2003). Wernicke's area is coupled to Broca's area located in the frontal lobe, which is responsible for motor speech output and is activated during auditory comprehension tasks.

The primary auditory cortex is most likely responsible for generating a number of evoked potentials (Musiek & Baran, 2007). The middle latency response (MLR) is likely generated by the primary auditory cortex, the thalamo-cortical pathway, and the reticular nuclei of the thalamus (Musiek & Baran, 2007). It has been suggested that the primary auditory cortex also generates late evoked potentials. Insults to the auditory cortex have resulted in compromised P300 and mismatch negativity (MMN) responses (Musiek & Baran, 2007).

### **Corpus callosum**

The corpus callosum is the largest fiber tract in the human brain and is primarily white matter. It is banana-shaped, measured to be about 6.5 cm long in an adult, and connects the two cerebral hemispheres with highly myelinated nerve fibers (Musiek, 1986b; Musiek & Baran, 2007). The cortex, discussed in the previous section, is very thin and lesions in the cortex also affect fibers of the corpus callosum. There are two

types of fibers in the corpus callosum: homolateral and heterolateral. Homolateral fibers connect one site in one hemisphere to the same site in the other hemisphere.

Heterolateral fibers, on the other hand, connect to different sites in each hemisphere after coursing through the corpus callosum (Musiek & Baran, 2007). Initially it was thought that most fibers in the corpus callosum were homolateral. In recent years many bundles of heterolateral fibers have been found in the occipital and temporal areas of the brain (Musiek & Baran, 2007).

Five areas make up the corpus callosum: the splenium, the trunk, the genu, the rostrum, and the anterior commissure (Musiek, 1986b). The splenium makes up approximately one-fifth of the corpus callosum and is considered the visual part of the corpus callosum with minimal auditory fibers (Musiek & Baran, 2007). The middle one-third of the corpus callosum is termed the trunk and is where somatosensory and motor fibers originating in the parietal lobe cross the midline. Animal studies have confirmed that the most posterior segment of the trunk encompasses the main auditory areas of the brain (Musiek, 1986b). Most fibers from the frontal lobe cross the midline in the anterior one-third of the corpus callosum, or the genu. The majority of the fibers in the rostrum have olfactory functions and the anterior commissure plays a role in pain and pain sensation as well as the sense of smell (Musiek & Baran, 2007).

The corpus callosum is responsible for the integration of information between the two hemispheres both within and across modalities. It also serves in an inhibitory way to prevent interhemispheric competition in selected tasks (Bellis, 2003). Without the corpus callosum, there would be a lack of communication between the two complementing hemispheres. In the human brain one hemisphere is dominant for one

process while the other is dominant for a different process. Without the interaction of the two hemispheres, optimal processing cannot be obtained (Musiek, 1986b).

### **Efferent pathways**

The efferent, or centrifugal, auditory pathway runs from the cortex to the hair cells in the cochlea paralleling the ascending auditory pathways (Musiek, 1986b; Bellis, 2003). The efferent system includes both excitatory and inhibitory functions and aids in the detection of a signal in background noise. The origin of this pathway is in the auditory cortex, where two efferent systems emerge. The first system descends to the MGB while the other descends to various auditory nuclei and hair cells of the cochlea (Musiek, 1986b). Efferent input from both the cortex and MGB is received in the IC. These signals then descend to the preolivary nuclei of the SOC as well as to the dorsal CN. There are some efferents that project to the nuclei of the LL, however, little is known about the anatomy and physiology of these projections.

The majority of research on the efferent system has been focused on the olivocochlear bundle, which, according to Bellis (2003), “extends from the SOC to the fibers beneath the hair cells of the cochlea” (p.47) and plays a role in the inhibition of the hair cells and the acoustic reflex. Two main descending tracts have been identified: the lateral olivocochlear (LOC) and medial olivocochlear (MOC; Guinan, 2006, Musiek, 1986b). The LOC efferent system contains mostly unmyelinated and uncrossed fibers originating from cells near the lateral segment of the SOC and terminating near the spiral ganglion beneath the inner hair cells of the cochlea. The MOC efferent system, on the other hand, originates at or near the preolivary nuclei medial to the medial superior olive and contains primarily myelinated, crossed fibers. This tract terminates in

the region of the inner hair cells as well. It has been hypothesized that the olivocochlear bundle is responsible for auditory attention, maintenance of optimal function of the cochlea, and assistance in coding of brief stimuli (Bellis, 2003).

This previously mentioned olivocochlear efferent system can be measured noninvasively in humans through contralateral suppression of OAEs. The MOC efferent system has been suggested to shift the dynamic range of hearing, protect from acoustic trauma, and aid in selective attention (Guinan, 2006). One additional suggested role of the MOC efferent system is to reduce the effects of masking noise. It has been demonstrated that the activity of the MOC efferent system enhances the encoding of signals in animals (Winslow & Sachs, 1988; Kawase & Liberman, 1993; May & Mequone, 1995) as well as in humans (Micheyl & Collet, 1996; Micheyl, Perrot, & Collet, 1997). This notion has been examined under both continuous and interrupted noise paradigms. Stuart and Butler (2012) found no significant correlations between the amount of contralateral suppression and performance in either continuous or interrupted noises suggesting that increased MOC efferent activity is not associated with improved speech perception in continuous and interrupted noise.

### **Acoustic Noise**

Noise exposure is the second leading cause of hearing loss after age-related hearing loss and is one of the most common occupational and environmental hazards (Rabinowitz, 2000). Noise exposure is also the most preventable contribution to hearing loss in the United States (Dobie, 2008). According to Rabinowitz (2000), more than 30 million Americans are exposed to potentially harmful noise levels each day in the workplace and even more Americans are affected by harmful noise levels in their

recreational activities. The NIDCD reports that approximately 26 million Americans have some degree of NIHL (NIDCD, 2014). This equates to roughly 15% of Americans between the ages of 20 and 69 as well as 16% of teenagers between 12 and 19 years of age.

Occupational and recreational noise exposure accounts for between an estimated 15% and 20% of the hearing loss burden in the United States (Dobie, 2008). It is quite difficult to determine the contribution of noise on hearing loss due to the similar pure tone audiometric features of NIHL and hearing loss due to aging. Both types of hearing loss most often consist of a bilateral hearing loss that is sensorineural in nature with high frequencies affected more than low frequencies. The hearing loss following noise exposure is often delayed making it very challenging to prevent. The heaviest burden of NIHL occurs in middle age and can appear decades following the exposure.

Noise exposure, in addition to loss in hearing sensitivity, can lead to a reduction in temporal summation, poor frequency resolution and speech discrimination, abnormally rapid loudness growth, and tinnitus in humans. This suggests that not only is the inner ear affected by intense noise exposure, so are the neural processes of the auditory system (Salvi et al., 1983). This work will focus on the effect of noise on peripheral auditory structures including the cochlea and auditory nerve.

Noise exposure can cause either temporary or permanent damage and is either the result of a one-time exposure to an intense noise or continuous exposure to loud sounds over an extended period of time. With proper regulations as provided by the



OSHA, NIHL is completely preventable. A discussion on different types of noise and its effect on cochlear structures will follow.

### **Types of Noise**

According to Goelzer et al. (2001), noise typing is determined by the variation of the frequency spectrum as a function of time. Specifically, noise can be classified into three types: steady, non-steady, and impulse. Steady noise is any noise with negligibly small fluctuations of sound pressure level within the observation period. To be considered steady the variations in amplitude between samples are less than 5 dBA (Goelzer et al., 2001). Non-steady noise, on the other hand, occurs when the sound pressure level varies significantly throughout the period of observation and can be further categorized as intermittent, fluctuating, or tonal noise. Finally, impulsive noise occurs when there is one or more burst of sound energy of high intensity with each burst having a short duration of less than one second. Impulse, or impact noise, can cause immediate mechanical alterations to the cochlea including tears in Reissner's membrane and almost total destruction of hair cells and supporting cells (Slepecky, 1986).

Both non-steady noise and impulsive noise can be further classified. Non-steady noise can be intermittent, fluctuating, or tonal. When the level of the noise drops to the level of the background noise several times during the observation and remains above the level of the background noise for at least a second it is considered to be intermittent, non-steady noise. According to Goelzer et al. (2001), fluctuating, non-steady noise is "a noise for which the level changes continuously and to a great extent during the period of observation" (p. 45). Tonal, non-steady noise is classified as one or two single

frequencies that can be either continuous or fluctuating. Impulsive noise is divided into type A and type B, or isolated impulse and similar impulses. An example of an isolated impulse would be a gunshot while an example of similar impulses is riveting.

**Temporary threshold shift.** The initial indication of damage due to noise exposure is a TTS. The noise contributing to a TTS has no morphological effect on the cochlea but can be attributed to metabolic changes with the outer hair cells of the cochlea, which are essential to hearing sensitivity and frequency selectivity and can be observed in the electrical response of the outer hair cells in the cochlea or by measuring changes to otoacoustic emission responses (Patuzzi, 1998; Quaranta et al., 2003). TTSs have been utilized as a safe test of susceptibility to permanent threshold shifts (PTS), which will be discussed below (Yates, Cody, & Johnstone, 1983).

For a TTS to be observed, the intensity of the noise must be greater than 70 dB sound pressure level (SPL) and the effects must be observed at least 2 minutes following cessation of the eliciting noise (Quaranta et al., 2003; Yates et al., 1983). TTSs will increase in a linear manner to the intensity of the noise up to 120 dB SPL where the TTS will then increase “logarithmically up to an asymptotic maximum known as the asymptotic threshold shift” (Quaranta et al., 2003, p. 164). The frequency spectrum of the noise determines the specific frequencies that are affected. Typically, in humans, the frequency range between 3000 Hz and 5000 Hz is most affected following intense noise exposure. This can partially be attributed to the ear resonance and the sound transfer function of the ear canal as previously discussed.

Depending on the intensity and duration of eliciting noise, thresholds can be temporarily elevated for minutes, hours, and days (Patuzzi, 1998). The onset and

recovery of a TTS is quite a complex process with a “multi-exponential” time course (Patuzzi, 1998, p. 39). There have been three proposed mechanisms behind a TTS and these include synaptic fatigue, metabolic fatigue of either the stria vascularis or HCs, and changes in blood flow. The pathophysiology of noise exposure resulting in a TTS will be discussed in detail below.

**Permanent threshold shift.** A PTS, as opposed to a TTS, is an irreversible hearing loss resulting from intense noise exposure (Martin & Clark, 2006). There is a direct correlation between the degree of PTS and the amount and location of damage to sensory cells in the inner ear (Clark, 1990). Following long-term, intense noise exposure damage can be observed in the inner ear including damage to the cochlea, OHC membranes, and changes to the size and shape of OHCs, as well as damage to the afferent dendrites contacting the IHCs (Fridberger et al., 2002; Moussavi-Najarkola et al., 2012). Some research has proposed that damage to OHCs is not always observed with PTSs. It has been suggested that when OHCs are not damaged, the permanent damage occurs in the reticular lamina and other structures important for fast motility (Wang et al., 2011). Most studies examining the effect of PTSs on animals have exhibited loss in sensitivity, broadening of the tuning curve, and a reduction in nonlinear response patterns (Salvi, Hamernik, & Henderson, 1983). PTSs are not the focus of this work and will not be discussed in detail.

### **Effects of Noise on the Animal Model**

The chinchilla is the most widely used animal in studies involving NIHL because of its lack of upper respiratory or middle ear infections and the availability to perform long term studies due to a longer lifespan of approximately twenty years (Clark, 1990).

Researchers have examined the effect of noise exposure on many other animals including cats (Heusden & Smoorenburg, 1981), guinea pigs (Canlon et al., 1987; Chan, Suneson, & Ulfendahl, 1998; Chen et al., 2003; Fridberger, 2002; Gao et al., 1992; Grenner, Nilsson, & Katbamna, 1989; Patuzzi, Yates, & Johnstone, 1989; Wang et al., 2011; Yates et al., 1983), mice (Shone et al., 1991), rats (Fraenkel, Freeman, & Sohmer, 2001), and gerbils (Gans, 1983). Much of what is currently known about the pathophysiology of NIHL has been deduced from animal research.

Most animal studies examining hair cell function follow a similar paradigm (Bohne, Harding, & Lee, 2007; Canlon et al., 1987; Chen et al., 2003; Gao et al., 1992; Nordmann, Bohne, & Harding, 2000). Typically, the experimental subject is exposed to noise of predetermined intensity, frequency, and duration that is known to elicit a change in cochlear function. Following exposure time, the animals are sacrificed and their temporal bones quickly removed while the cochleae are carefully harvested. The cochleae are then soaked in solution and shortly thereafter dissected. During dissection the status of the stereocilia and hair cells is carefully examined with use of an optical microscope. Researchers examining the effect of noise exposure on the compound action potential in animals also follow a similar paradigm. In these studies, the experimental animals are exposed to the eliciting stimuli and then anesthetized for recordings. Most often a silver ball electrode is then placed on the round window niche of the cochlea or on the cochlear bone adjacent to the round window (Kujawa & Liberman, 2009; Salvi et al., 1983; Yates et al., 1983). ABRs are then recorded and compound action potential thresholds are identified. Elevations in compound action potential thresholds are often observed.

**Noise and hair cells.** Morphological evidence from animal studies suggests that damage occurs in a number of locations following noise exposure including: the sites responsible for electro-mechanical transduction including HC stereocilia and links, reticular lamina, and tectorial membrane; OHCs; neuronal innervations; stria vascularis; and fibrocytes (Wang et al., 2011). There have been numerous studies specifically examining the effect of noise on HC stereocilia (Canlon et al., 1987; Gao et al., 1992; Nordmann, Bohne, & Harding, 2000; Wang et al., 2011) and sensory cells (Bohne, Harding, & Lee, 2007; Chan et al., 1998; Chen et al., 2003; Clark, 1990; Fridberger et al., 2002; Patuzzi et al., 1989).

Hypotheses regarding the mechanism of NIHL include mechanical damage, ischemia, excitotoxic damage, metabolic exhaustion, and ionic imbalance to inner ear fluids. Nordmann et al. (2000) exposed chinchillas to 24 hours of an octave band noise centered around 4,000 Hz and presented at 86 dB SPL. The animals exhibiting a TTS were found to have buckling of the pillar bodies in the cochlea as well as uncoupling of OHC stereocilia from the tectorial membrane. Four animals in this study exhibited PTSs from the noise exposure. In three of these animals, focal losses of HCs and adjacent afferent nerve fibers were identified. Comparatively, Wang et al. (2011) exposed albino guinea pigs to broadband noise at 110 dB SPL for 2 hours. It was found that following only this moderate noise exposure stereocilia of HCs largely recovered their architectural organization.

Canlon et al. (1987) measured micromechanical properties of HC stereocilia following noise exposure known to produce a PTS. Pigmented guinea pigs were exposed bilaterally to a 1,000 Hz pure tone for 1, 24, 72, 120, or 168 hours.

Micromechanical measures were then observed directly following noise exposure or after a 6-week recovery period. The micromechanical measurements were made in turns 2, 3, or 4 of different cochleae. It was found for the pigmented guinea pigs observed directly following exposure that IHCs had a decrease in threshold of approximately 7 dB and became less stiff following noise exposure. This suggests that the IHC stereocilia require less force to initiate movement. Thresholds of the three rows of OHCs did not change following the noise exposure. Following the 6-week recovery period the IHCs were found to restore with thresholds approaching control values. All but a few IHCs were intact with normal appearing stereocilia.

Gao et al. (1992) compared changes in the stereocilia of albino guinea pigs with TTSs and PTSs. A 30-minute exposure to 110 dB broadband noise produced a TTS while a 150-minute exposure to 120 dB broadband noise produced a PTS. It was found that the lesion following a TTS was restricted to the third row of OHCs. The PTS, on the other hand, exhibited an extensive lesion from the basal to second turn of the cochlea. In the group of guinea pigs with a PTS, either all three rows of OHCs or the IHCs and first row of OHCs had abnormal stereocilia. During a TTS the damaged stereocilia displayed bending and separation of the tips with no injury to the base or trunk. Any displacement or disarray was associated with PTSs.

A correlation between the amount of permanent hearing loss and the extent and location of damage to sensory cells has been shown to exist (Clark, 1990). Many studies prior to 1989 have suggested that OHC disruption is the primary cause of TTSs following noise exposure. Previous studies have suggested temporary depolarization of OHCs correlates with TTSs due to the fact that OHC membrane potentials and auditory

thresholds recover in the same manner following noise exposure (Cody & Russell, 1985). Patuzzi et al. (1989) examined if any correlation between mechanical sensitivity of the BM and the electro-mechanical transduction efficiency of the OHCs exists. The gross microphonic (200 Hz) of the basal turn of the cochlea was utilized to examine the integrity of the electro-mechanical transduction of the OHCs since the OHC receptor currents dominate the cochlear microphonic. To evaluate the mechanical sensitivity of the BM the compound AP visual detection threshold was observed, as there is good correlation between neural sensitivity and BM mechanical sensitivity at its characteristic frequency. Fifty-three mixed-strain guinea pigs were used in this study. It was determined that there is a good correlation between the residual microphonic amplitude and the mean compound AP elevation following noise exposure. The low frequency microphonic was decreased in amplitude following acoustic overstimulation. Patuzzi et al. (1989) suggested that this could result from a number of possible causes including a low frequency reduction in transverse organ vibrations; changes in stiffness of the OHC stereocilia; a reduction in the electro-mechanical transduction efficiency of the OHC due to changes in the K<sup>+</sup> gating mechanism; or an electrical change in the cochlea affecting the filtering of the microphonic.

Following insult, cells go through a number of changes that represent a disease process and have been identified as death pathways. These changes are the earliest indicators of important toxic reactions to trauma including noise exposure. The gold standard for discriminating between the death pathways is by examining the morphological appearance of the dying cells. Trump et al. (1997) identifies the three common cell death pathways as oncosis, apoptosis, and necrosis. According to Trump

et al. (1997), marked alterations in cell shape and volume can be observed during oncosis, including the tissues appearing opaque and often described as “cloudy swelling” (p. 81). These cells ultimately rupture, at which point they are termed necrotic (Bohne et al., 2007). Apoptotic cells, on the other hand, are shrunken and lose their attachments to adjacent cells and evoke no inflammatory response.

Three cell death pathways have specifically been identified in OHCs in chinchilla organs of Corti that have been exposed to octave band noises centered at 500 Hz and 4,000 Hz (Bohne et al., 2007). These pathways include the previous mentioned oncotic and apoptotic death pathways as well as a newly defined pathway. Most of the OHCs after noise exposure follow neither oncotic nor apoptotic death pathways but the third death pathway, which is morphologically distinct from the other two death pathways. This pathway is described as OHCs having no basolateral membrane but cellular debris in the shape of an intact OHC with a nucleus deficient in nucleoplasm. Bohne et al. (2007) suggested that following moderate noise exposure OHCs appear damaged “as if they were turning over more rapidly than normal” (p. 69).

Chan et al. (1998) examined the noise-induced alterations to the sensory cells in pigmented guinea pigs exposed to impulse noise. The noise exposure produced significantly lower axial stiffness of the OHCs than the control group having received no impulse noise exposure. A trend of recovery of axial stiffness was observed in animals at 1 and 2 weeks post noise exposure. Shorter HCs located at the apical end of the cochlea are more susceptible to noise-induced trauma than longer HCs located at the basal end of the cochlea. Chan et al. (1998) did find that the effect of noise exposure was indeed more evident in the shorter HCs and that “acoustic overstimulation causes



significant reduction in the stiffness of the outer hair cells accompanied by a reduction in cell length” (Chan et al., 1998, p. 967).

Similar to the Chan et al. (1998) study, Chen et al. (2003) explored the vulnerability of OHCs and IHCs to acoustic trauma. Albino guinea pigs were exposed to a pink noise at  $106 \pm 2$  dB SPL for 44 hours. Animals were then observed 1, 4, 7, 14, 21, and 63 days post noise exposure. Twenty-four hours following exposure, scattered damage was found throughout the cochlea with most prominent damage in the second and third turns of the cochlea. IHC stereocilia were bent, fused, or collapsed while the OHCs exhibited minor changes such as a few fused or bent stereocilia with the first row of OHCs unaffected. At 4 days post exposure, the IHC stereocilia were fused moderately and collapsed more completely than at 24 hours and the first row of OHCs were still unaffected. Seven days after noise exposure, some of the IHC stereocilia were lost and damage was observed in rows 2 and 3 of the OHCs. Fourteen days after exposure damage was observed in all rows of HCs except for the first row of OHCs. By 21 days post exposure, the OHCs began to show repair while the IHC stereocilia were still fused, bent, or collapsed. Finally, by 63 days, all rows of HCs exhibited repair.

Additionally, Fridberger et al. (2002) described alterations of cochlear function of pigmented guinea pigs following repeated 100-112 dB SPL tone bursts by examining BM vibrations. BM vibrations following noise exposure were transiently reduced with recovery occurring over the course of approximately 50 ms. Fridberger et al. (2002) suggest that the reduction in BM velocity was due to changes in cochlear amplification, which is determined by the passive mechanical properties of the inner ear.

**Noise and the action potential.** The AP has been utilized in animal studies examining effects of noise exposure to help determine the frequency specific state of the cochlea. It has been proposed that behavioral thresholds may not be an accurate and sensitive indicator for underlying HC lesions and that perhaps the AP is more sensitive and susceptible to acoustic trauma than behavioral thresholds or the CM (Heusden & Smoorenburg, 1981; Salvi et al., 1983).

Heusden and Smoorenburg (1981) studied the effects of noise trauma on the 8<sup>th</sup> nerve AP to determine frequency specificity of the cochlea in cats. The AP evoking stimulus in this study was a single-frequency tone-burst and the noise exposure was a 30 minute broadband noise presented at 105.3 dB SPL, which was known to produce a long lasting TTS. A recording electrode was placed in the vicinity of the round window ipsilateral to the stimulus ear. The results of this study indicated that AP thresholds are higher than behavioral thresholds and single fiber thresholds following acoustic trauma. The greatest threshold shift following the broadband noise exposure was observed between 2,000 Hz and 6,000 Hz. No significant change was observed in AP latency values at threshold when comparing responses pre- and post-noise exposure.

Changes in single neuron firing patterns have often been observed in animals with noise trauma. Salvi et al. (1983) examined the effects of noise exposure on the response properties of auditory nerve fibers. Twenty chinchillas were exposed to five days of 95 dB SPL octave band noise centered around 500 Hz. This noise exposure was known to produce an asymptotic TTS. The response properties of auditory nerve fibers following noise exposure were then related to the audiometric profile and any histological changes noted in the cochlea. Eight of the 20 chinchilla were utilized to

establish normative data. Six chinchilla were behaviorally trained to obtain threshold data and the remaining six were used for AP and single fiber measurements. Salvi et al. (1983) found that behavioral thresholds gradually increased and reached an asymptotic level by 24 hours post noise exposure except for 8,000 Hz and 16,000 Hz, which required approximately two days to reach a stable level. Behavioral thresholds were also approximately 10 dB lower than neuronal thresholds across most of the frequency range. It was expected that the hearing loss as a result of the narrowband noises utilized in this study would produce the greatest threshold shift around one-half to one octave above the provoking noise. This held true in the initial stage of TTS; however, as the exposure progressed, the hearing loss became relatively flat with the high frequency thresholds increasing as well. Salvi et al. (1983) also found that the AP recovered about 10-15 dB of sensitivity, which was very similar to the recovery of behavioral thresholds. Finally, auditory nerve fibers exhibited a loss in sensitivity and decrease in tuning following a TTS.

The recovery of AP thresholds following TTS and the phenomenon of forward masking has also been compared (Yates et al., 1983). The phenomenon of forward masking is “a short-lived elevation of auditory threshold which accompanies brief and/or less intense stimuli” (Yates et al., 1983, p. 306). In this study the post-stimulus elevation of AP thresholds was examined in 33 pigmented guinea pigs. A recording electrode was placed on the cochlear bone adjacent to the round window. The noise stimuli were 10,000 Hz tone bursts at intervals of 25 ms, 250 ms, or 1,000 ms presented at an intensity of 90 or 100 dB SPL. It was concluded that the recovery following the short, intense noise exposure occurs in as many as four different stages lasting a total

of slightly over 20 s. The two most prominent stages occur in 10 - 100 ms and 100 - 1,000 ms. The other two stages last 2 - 6 ms and greater than 20 s. It was found that the more intense the noise was, the greater the threshold shift and the longer the recovery.

Kujawa and Liberman (2009) examined the consequences of noise exposure on afferent nerve terminals and the cochlear nerve. In this study mice were exposed to an octave band noise (8000-16000 Hz) presented at 100 dB SPL for 2 hours. This exposure is known to produce a moderate, but reversible, threshold shift. ABR testing was performed with the compound AP threshold being identified, as well as DPOAEs. The mice were then sacrificed and confocal imaging of the sensory epithelium was utilized to quantify degeneration of cochlear hair cells, nerve terminals, and the synapses that connect them. This study found that AP threshold responses returned to pre-exposure thresholds; however, suprathreshold measures only returned to approximately 40% of pre-exposure levels. DPOAE responses, on the other hand, recovered completely at all test frequencies tested. Confocal imaging revealed no loss of hair cells at any post-exposure time out to at least one year. It did, however, reveal significant degeneration of both presynaptic and postsynaptic elements in the IHC area through the basal turn of the cochlea. These changes included a decrease in the number of presynaptic ribbons with many remaining ribbons appearing abnormally large, and a reduction in fiber density in the IHC area in proportion to the loss of ribbons. Kujawa and Liberman (2009) suggest that normal threshold sensitivity following noise exposure “can mask ongoing and dramatic neural degeneration in noise-exposure ears” (p. 14083). This reversibility of noise-induced threshold shifts appears

to be masking underlying neuropathology that likely has a long-term effect on auditory processing including hearing in noise, tinnitus, and hyperacusis.

### **Effects of Noise on Humans**

A generalization of the effects of noise exposure on the cochlea include possible tears in Reissner's membrane and the basilar membrane, focal lesions with almost total destruction along the sensory epithelium, and, after longer times post-exposure, missing HCs and supporting cells (Slepecky, 1986). With intense impulse noise the middle ear may be damaged with a torn TM resulting in ineffective conduction of the acoustic signal. Due to the fact that the organ of Corti is often damaged, the BM motion and micromechanic properties of the remaining HC stereocilia and tectorial membrane interactions may also be affected. There are also secondary alterations in the inner ear following noise exposure. These include an intermixing of cochlear fluids, a change in the metabolism of the remaining supporting and sensory cells, and a disruption in the blood flow of the inner ear (Slepecky, 1986). A simple relation does not exist between exposure intensity and the extent of structural damage, however, it is known that for a given intensity the amount of damage to inner ear structures at 30 days post exposure increases as the time of exposure increases.

Shortly following noise exposure in humans OHCs are swollen with an accumulation of lysosomes, vacuolization of the endoplasmic reticulum, and an increase in Hensen bodies (Slepecky, 1986). According to Slepecky (1986), stereocilia clump and fuse immediately following noise exposure and these effects can last days or even years. Temporary effects on stereocilia include appearing floppy and having cross-bridges between actin filaments broken. HC bodies often become distorted with

debris found scattered in the scala media. The tectorial membrane, however, seems resistant to damage from noise exposure.

The minimum structural damage resulting in threshold shifts occurs at the level of HC stereocilia. Both IHC and OHC stereocilia damage has been correlated with changes in behavioral thresholds and N1 thresholds with the progression of damage being disarray, to partial fusion or loss, to total fusion or loss. As the damage progresses, so does the degree of threshold shift (Slepecky, 1986).

It is thought that the immediate damage to stereocilia is mechanical in origin, resulting from the stereocilia of one cell colliding with another. As mentioned previously, the secondary effects to the remaining cells may be caused by an intermixing of cochlear fluids, ischemia due to changes in the vascular system, changes to supporting cells, or general metabolic changes caused by overstimulation. Cochlear fluids may intermix due to an alteration in tight cell junctions at the reticular lamina or holes that appear in the reticular lamina with both mechanisms providing a route between the endolymphatic space and fluid space of the organ of Corti. Sensory cells may also experience damage from exhaustion “due to increased load on the sensory cells, resulting in depletion of enzymes and metabolites, coupled to an insufficient or decreased circulation in the sensory regions” (Slepecky, 1986, p. 313). Noise exposure causes mechanical destruction to the HCs and supporting cells in the organ of Corti with some effects on blood flow. Intense metabolic activity alters the cellular redox state and has also been known to contribute to NIHL. This ultimately leads to increases in mitochondrial free radical formation (LePrell et al., 2007). According to LePrell et al. (2007), in excess these formations “damage cellular lipids, proteins, and DNA, and

upregulate apoptotic pathways” (p. 22). As discussed previously, apoptotic cells are shrunken and lose their attachments to adjacent cells and evoke no inflammatory response.

The damage to HCs in humans following noise exposure is immediate, mostly permanent, and correlates with functional loss (Slepecky, 1986). The types of damage to stereocilia include fusion and disarray. OHCs are more susceptible to damage than IHCs, which is most likely due to structural reasons. IHCs are located closer to the osseous spiral lamina, which does not respond as much to BM motion and are surrounded by supporting cells. OHCs, on the other hand, are coupled to the motion of the BM, are connected to the tectorial membrane through the tallest stereocilia, and are not surrounded by supporting cells leading to more exposure to BM motion (Slepecky, 1986). Following histopathological evaluation of temporal bones after noise exposure resulting in PTSs, McGill and Schuknecht (1976) found morphological changes mainly consisting of HC loss with greater loss of OHCs than IHCs.

### **Individual Susceptibility to Noise-Induced Hearing Loss**

It has been well demonstrated that frequency, duration, and intensity all determine the amount of TTS exhibited following noise exposure. In addition to the frequency, duration, and intensity composition of noise exposure, there is a wide range of biological and nonauditory factors that can contribute to susceptibility of an individual to NIHL. Henderson, Subramaniam, and Boettcher (1993) reported on a number of biological factors contributing to susceptibility of NIHL including eye color, gender, age, and smoking habits, as well as confounding factors including ototoxic drug use and

environmental agents. Other factors contributing to NIHL include anatomical variation in auditory periphery and psychological stress (Hooks-Horton, Geer, & Stuart, 2001).

NIHL research on its relation to eye color has shown that blue-eyed individuals are more susceptible to NIHL than those with more melanin content in their eyes (Henderson et al., 1993). A “sensitive period” directly following birth of animals has been proposed as a time during development when animals are more susceptible to NIHL. The “sensitive period” has been compared to the third trimester in human pregnancies. It has been found that exposure to noise in utero can result in NIHL. Smoking has also been shown to lead to an increase in susceptibility to NIHL. This has been attributed to the carbon monoxide in smoke; however, the exact relation between NIHL and smoking is hard to define due to the numerous health conditions associated with smoking (Henderson et al., 1993).

Aminoglycoside antibiotics and antineoplastic agents often exacerbate NIHL (Henderson et al., 1993). Doses of aminoglycoside antibiotics including gentamicin, kanamycin, and neomycin will lead to NIHL and HC losses. Similarly, the antineoplastic agent cisplatin also causes hearing and HC losses. These medications can be ototoxic and can interact significantly with noise, causing greater hearing loss than caused by either agent alone. Toluene, a common solvent used in paint and an airborne toxin in many occupational environments may also exacerbate the effects of noise. This particular solvent causes high frequency hearing loss that is greater than exposure to noise alone. Carbon monoxide, carbon disulphide, lead, and trimethyltin have also been shown to interact with noise exposure leading to an increase in the amount of NIHL a worker may experience.



It has been proposed that exercise contributes to an individual's susceptibility to TTSs with an increase in the amount of shift with exercise relative to noise exposure alone. Changes in metabolic activity including an increase in core body temperature and the release of catecholamines, as well as depression of the stapedius reflex have been proposed as possible explanations for this relationship (Hooks-Horton et al., 2001). Similarly, some studies have suggested that this relationship between TTSs as a result of noise exposure and exercise compared to noise alone does not exist.

Hooks-Horton et al. (2001) examined the effects of noise and exercise together and individually on cochlear function as assessed by behavioral thresholds and DPOAEs. Gender and ear effects were also considered. The participant pool included 8 normal hearing males and 8 normal hearing females. Four pure tone frequencies including 2000, 3000, 4000 and 6000 Hz were utilized as test frequencies. The noise stimulus was a 105 A-weighted decibel [dB(A)] 2000 Hz narrowband noise for a duration of 10 minutes. This study found that there were significant elevations in thresholds and significant reductions in DPOAE levels for the 2 conditions with noise exposure. Exercise in combination with noise exposure, however, did not exacerbate the TTSs or reduction in DPOAE levels when compared to noise exposure alone. No significant effects of gender or ear on TTSs were identified in this study.

Other research studies have suggested that there are gender effects on the susceptibility to NIHL. Ward (1966) found that following exposure to low frequency noises below 700 Hz males had 30% more TTS than females. Comparatively, following exposure to high frequency noises, males had 30% less TTS than females. These results led to the hypothesis that females have "more efficient middle ear muscles"

(Ward, 1966, p. 485) suggesting that the transmission of low frequency energy is reduced while high frequency energy transmission is enhanced with strong contraction of the middle ear muscles. Petiot and Parrot (1984) observed absolute thresholds following noise exposure in young women during the pre-ovulatory phase and menstrual phase as well as young woman in the same phases while taking oral contraceptives and one group of young men for gender comparisons. No differences in absolute threshold between men and women were observed, however, females on oral contraceptives had significantly lower resting thresholds, larger TTSs, and higher recovery rates than males and females not taking contraceptives. Hori, Nakashima, and Sato (1993) compared TTSs of women versus men and compared TTSs of women in different phases of the menstrual cycle. Larger TTSs were observed at 3000 and 4000 Hz and smaller TTSs were observed at 6000 Hz for males when compared to women in all phases of the menstrual cycle. Previous studies have also reported that the greatest PTS occurs at 4000 Hz for men and 6000-8000 Hz for women (Hori et al., 1993).

### **Assessment of Hearing**

As discussed previously, the hearing system is comprised of peripheral and central structures that contribute to the ability to hear. It is essential to have an understanding of the various tests utilized to assess both peripheral and central auditory function. This section will focus primarily on peripheral auditory assessment with a brief discussion of central auditory assessment, as this is not the focus of this work.

#### **Peripheral Auditory Assessment**

The decoding of the auditory signal begins in the periphery with the transduction of the signal from acoustic to mechanical to hydraulic energy as it travels from the outer

ear to middle ear and finally to the inner ear. The primary goal of peripheral assessment is to evaluate the integrity of these structures.

**Pure tone audiometry.** Hearing sensitivity is assessed behaviorally by pure tone air and bone conduction audiometry. The American Speech-Language Hearing Association (ASHA; 2005) offers a document listing the guidelines for pure tone threshold testing that are most widely used in clinical settings. ASHA (2005) defines pure tone threshold audiometry as a “measurement of an individual’s hearing sensitivity for calibrated pure tones” (p. 1). Three general methods including manual, automatic, and computerized are used for pure tone audiometry with the most popular being the manual method. From this point forward pure tone audiometry will be referring to the manual method.

Prior to any testing the audiometer must be calibrated and functioning properly to assure accurate test results. The audiometer and transducers must meet the requirements set forth by the American National Standards Institute (American National Standards Institute, 2004). Equipment should be electro-acoustically calibrated annually with functional inspections and listening checks occurring daily. Supra-aural headphones and insert earphones are appropriate transducers for air conduction testing from 125 Hz to 8000 Hz. Bone conductors are appropriate for bone conduction testing within their respected frequency response range as long as specifications of *Mechanical Coupler for Measurement of Bone Vibrators* are met (ANSI S3.13-1987, American National Standards Institute, 2002). Transducers should not be interchanged without appropriate recalibrations.

Patients should be seated in a chair in a quiet room with the audiologist properly placing the appropriate transducers. A sound-attenuated or sound-isolated booth is the most commonly accepted room for audiometric testing. Instructions are given to the patient explaining the purpose of the test, how the patient is to respond, and clarifying any questions the patient may have. Patient response is often obtained by having the patient raise his hand or press a button. It is essential to avoid giving inadvertent visual cues to the patient during testing.

Pure tone air conduction thresholds are recommended to be measured at 250, 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hz except when a low-frequency hearing loss exists at which time 125 Hz would also be measured (ASHA, 2005). Typically, pure tone air conduction testing begins at 1000 Hz with the presentation of the tone at 30 dB HL. If no response is obtained the presentation level is increased to 50 dB HL and to successive additional increments of 10 dB until a response is obtained. According to ASHA (2005), “threshold is defined as the lowest decibel hearing level at which responses occur in at least one half of a series of ascending trials” (p. 5). Once an initial response is obtained the presentation level is decreased in 10 dB increments until no response at which point the level is increased in 5 dB steps. Testing begins with the better ear when this information is available. An intensity level is deemed a threshold when two responses are obtained out of three presentations at a single level (American National Standards Institute, 2004). Pure tone bone conduction thresholds are obtained in the same manner as air conduction thresholds.

Air conduction thresholds are obtained as a result of the signal passing through the entire auditory system. Typically, either an insert earphone or supra-aural earphone

is placed in or around the pinna and sound is passed through the outer ear to the TM, through the middle ear system by mechanical transduction of energy across the ossicles, and into the inner ear via hydraulic energy as the fluid is set into motion in the cochlea. Once here, the signal travels up the auditory nerve and through the central auditory pathway. This initial test signal is an acoustic signal. Bone conduction thresholds, on the other hand, are obtained by the vibration of the bone oscillator against the skull. The most popular placements of the bone oscillator are either the forehead or mastoid bone. Bone conduction testing allows for the signal to bypass the outer and middle ear, directly stimulating the traveling wave in the cochlea. By comparing air conduction thresholds to bone conduction thresholds one can better determine the site of hearing loss.

Pure tone testing can provide information about the integrity of the auditory system. Threshold levels can be classified as multiple severities of hearing loss. According to Goodman (1965), thresholds between -10 dB HL and 25 dB HL are considered normal, 26 dB HL to 40 dB HL are mild, 41 dB HL to 55 dB HL are moderate, 56 dB HL to 70 dB HL are moderately severe, 71 dB HL to 90 dB HL are severe, and 91 dB HL and higher are profound. In addition to the severity of loss, there is also a type of hearing loss. If both air conduction thresholds and bone conduction thresholds are within 10 dB of each other and outside of the normal range, the hearing loss is considered sensorineural in nature. If the air conduction thresholds are outside the normal range while the bone conduction thresholds are normal, the hearing loss is considered conductive in nature. Finally, if both air conduction and bone conduction thresholds are outside of the normal range but the bone conduction thresholds are

greater than 10 dB better than air conduction thresholds, the hearing loss is mixed in nature.

Pure tone audiometry is a stable measure of auditory integrity (Landry & Green, 1999; Stuart et al., 1991). Stuart et al. (1991) examined test-retest variability in audiometric thresholds using both supra-aural and insert earphones in children between 6 and 13 years of age as well as in young adults. It was determined that there is no difference in the test-retest variability between adults and children or in supra-aural versus insert earphones. There is greater variability in extremely low and extremely high frequencies. The major contributing factors to an increase in variability of thresholds are subjective factors including physiological and psychological effects (Stuart, 1991). Individual motivation, fatigue, attention, adaptation, and familiarization can lead to an increase in variability. It would be expected that children would be more susceptible to these effects; however, this is not the case. Stuart et al. (1991) found that children only had an increase in test-retest variability at 250 Hz when compared to young adults.

Chermak, Dengerink, and Dengerink (1983) examined the test-retest reliability of auditory threshold and TTS measures in normal hearing college-age males and females with no history of ear disease. The eliciting noise stimulus was a 3-minute, 110 dB SPL white noise. The assessment of auditory thresholds was found to be a reliable measure; however, changes in hearing sensitivity must be considered. TTSs were also deemed reliable measures when obtained within the same session. For this study the same session was considered to be within 30 minutes. It was noted that over a 1-week time span TTS reliability was lost.

**Speech testing.** Speech audiometry is another assessment of peripheral and central auditory function that specifically includes assessment of the threshold for which an individual can hear speech and serves as a validity check to the pure tone audiogram (ASHA, 1988). According to ASHA (1988), a “speech recognition threshold (SRT) is the minimal level for speech at which an individual can recognize 50% of the speech material” (p. 3). Test materials for this type of speech testing include spondaic words, which are two syllable words with equal stress on each syllable. Typically, during speech audiometry patients either repeat or point to the correct speech material. To determine SRT values, ASHA (1988) recommends that a starting level be identified. Initially it is recommended to begin the process of determining a starting level by presenting spondaic words 30 to 40 dB sensation level (SL) relative to the three frequency pure tone average, or average of air conduction thresholds at 500 Hz, 1000 Hz, and 2000 Hz. With each correct response the intensity is decreased by 10 dB HL until two consecutive words are missed. Once this occurs, the intensity is increased by 10 dB HL and this is the starting level. To determine the SRT two spondees would be presented at the starting level and then at each successive two dB decrement until five out of six responses are incorrect. The SRT is then calculated by using the formula  $SRT = \text{starting level} - \# \text{ correct} + \text{correction factor}$ . The correction factor for determining the SRT is +1 dB. This value is then compared to the three-frequency pure tone average from the audiogram. The most common reasons for obtaining SRTs are three-fold: providing a cross-validation for pure tone thresholds, measuring communication disability, and use as a reference for suprathreshold word recognition testing (McArdle & Hnath-Chisolm, 2009). SRTs are considered in good agreement with pure tone

averages if the difference between the two values does not exceed 10 dB (Schlauch & Nelson, 2009). This difference may change depending on the configuration of the audiogram.

**Suprathreshold word recognition testing.** Speech recognition in quiet is also evaluated when the speech materials are presented at a predetermined level suprathreshold to the previously obtained SRT. This level should be loud enough to obtain the maximal score and is a highly variable measure from patient to patient. Typically, word recognition test material is presented at 30 to 40 dB SL relative to the SRT (McArdle & Hnath-Chisolm, 2009). Word recognition testing has also been utilized for obtaining a performance-intensity function, or psychometric function, of percent correct for a given number of speech stimuli at different presentation levels. By examining these functions audiologists can better differentiate between cochlear hearing loss and retrocochlear hearing loss (McArdle & Hnath-Chisolm, 2009).

Several types of speech material can be utilized for word recognition testing including sentences, nonsense syllables, and monosyllabic words. McArdle and Hnath-Chisolm (2009) suggest that the most difficult stimuli for word recognition testing are nonsense syllables while sentences are the easiest stimuli. Monosyllabic words; however, are the most commonly utilized. Numerous monosyllabic word lists have been developed for word recognition testing in the audiology clinic. These lists were developed based on strict criteria that they were monosyllabic in nature, have an equal average difficulty, range of difficulty, and phonetic composition of lists, be a representative sample of American English, and be familiar words. The Northwestern University Auditory Test Number 6 (NU No. 6), the CID Auditory Test W-22 (CID W-22),



and the Phonetically Balanced 50 (PB-50) all meet the above listed criteria for adult listeners (McArdle & Hnath-Chisolm, 2009).

**Tympanometry.** Tympanometry is “a measure of acoustic immittance in the ear canal as a function of varying air pressure within the ear canal” and is used to assess middle ear function (Keefe & Feeney, 2009, p. 143). This is accomplished by tracking admittance of the middle ear system during changes in ear canal pressure with a middle ear analyzer. A middle ear analyzer must contain a probe that houses a loudspeaker to elicit the 226 Hz probe tone, a microphone to monitor the level of the probe tone, and a pump to change ear canal pressure. The ultimate goal of tympanometry is to determine the point and magnitude of greatest compliance of the TM (Martin & Clark, 2006).

Prior to recording a tympanogram the audiologist must select and place an appropriate sized probe into the opening of the ear canal so as to provide a hermetic seal. The hermetic seal allows for air pressure changes to be transferred to the TM. Once the seal is obtained the pressure sweep is typically begun at +200 dekapascal (daPa) and swept to -400 daPa all the while making measurements of compliance. The information obtained is displayed in a graph, which contains four important indices of middle ear function: ear canal volume ( $V_{ea}$ ), peak compensated static acoustic admittance ( $Y_{tm}$ ), tympanometric peak pressure (TPP), and tympanometric width (TW; Keefe & Feeney, 2009). These indices all contribute to assessment of middle ear function.  $V_{ea}$  can be useful in evaluating if a tympanostomy tube is patent or blocked and whether the TM is intact or not. Significant negative TPP can often suggest Eustachian tube dysfunction. Abnormally low  $Y_{tm}$  indicates an abnormally stiff middle ear and can suggest certain pathologies including middle ear effusion, otosclerosis, a

thickened eardrum, and malleous fixation. On the other hand, an abnormally high  $Y_{tm}$  only requires medical referral if a significant conductive or mixed hearing loss is identified on the audiogram (Shanks & Shohet, 2009). According to Shanks and Shohet (2009), TW has been useful in identifying ears with middle ear effusion. Typically, these tympanograms are quite broad and rounded with a larger TW than tympanograms of normal middle ear systems. Roup et al. (1998) suggest that normal tympanometric values are as follows for young (20 to 30 years old), normal hearing adults:  $Y_{tm}$  values between 0.30 and 1.50 millimhos (mmhos),  $V_{ea}$  values between 0.90 and 1.80 cm<sup>3</sup>, and TW values between 35.80-95.00 daPa. By combining the above mentioned middle ear indices, a clinician is better prepared to make statements regarding middle ear function than with the audiogram alone.

Tympanometric results can also predict results for other audiometric tests. OAE testing, for example, relies on the transmission of the response from the cochlea to the ear canal. The middle ear status can directly affect the presence or absence of the response (Avan et al., 2000; Yeo et al., 2002). Yeo et al. (2002) found that middle ear effusion significantly affected the expression rate of spontaneous otoacoustic emissions (SOAEs), transient evoked otoacoustic emissions (TEOAEs), and DPOAEs.

**Acoustic reflex testing.** Acoustic reflex testing is performed in the clinical setting to assess the acoustic reflex arc resulting in contraction of the stapedius muscle, which, in turn, stiffens the middle ear transmission system (Gelfand, 2009). This pathway has been discussed in detail previously and will be reviewed briefly prior to a description of how reflex thresholds are measured.

As described previously, the stapedius reflex is primarily thought to protect the ear from intense sounds more than 75 dB above the absolute threshold and can also be activated by vocalization, tactile stimulation of the head, or general body movement, as well as in some humans without any other discernible movements (Lee et al., 2006; Pickles, 2008). There are ipsilateral (uncrossed) and contralateral (crossed) reflex pathways resulting in four distinguishable reflex arcs (Gelfand, 2009). Several functions have been suggested for the acoustic reflex including inner ear protection from noise damage, ability to keep intense low-frequency stimuli near a lower part of the intensity range, a beneficial effect on the frequency response of the middle ear, and a reduction in the masking effect of low frequency noise (Pickles, 2008).

As the reflex response of the stapedius muscle results in a change in the immittance of the middle ear system, the same instrumentation utilized for tympanometry will be required to measure acoustic reflex responses. A probe with a 226 Hz probe tone is placed in the ear canal and a hermetic seal is obtained. This will allow the reflex to be obtained at the point of TPP (Gelfand, 2009). The eliciting stimuli are most often tonal stimuli at 500 Hz, 1000 Hz, and 2000 Hz, as well as broadband noise. Reflexes have been obtained to 4000 Hz tonal stimuli, however, this is not recommended as many normal hearing young adults experience elevated reflexes at 4000 Hz. Once the hermetic seal is obtained the chosen tonal or broadband stimuli is presented to one ear while changes in compliance are monitored at either the stimulus ear or at the contralateral ear. Traditionally stimuli presentation levels are increased by 5 dB until a decrease in compliance of at least 0.2 ml is noted. If truly an acoustic reflex, this decrease in compliance will increase in magnitude with an increase in

intensity of the eliciting stimuli. Normal acoustic reflex thresholds range from 85 dB SPL to 100 dB SPL for pure tone stimuli and approximately 20 dB lower for broadband stimuli (Gelfand, 2009).

It has been proposed that the stapedius acoustic reflex protects the ear from intense sounds. Zakrisson et al. (1980) examined the protective mechanism of the stapedius muscle contraction in Bell's palsy patients with unilateral facial nerve dysfunction resulting in paralysis of the stapedius muscle. These patients were exposed to shipyard noise at 102 dB(A) for fifteen minutes, which resulted in a TTS. Shortly following the noise exposure substantially greater threshold shifts were recorded on the affected side than the unaffected side. Similarly, poorer thresholds have been observed in rabbits with deactivated stapedius muscles exposed to shipyard noise eliciting a PTS than their normal counterparts (Henderson, 1993). Researchers have also suggested that individuals with a history of noise exposure could have normal acoustic reflex thresholds with other abnormal reflex indices including decreased amplitude and faster decay at suprathreshold levels (Henderson, 1993). A similar study examining the effects of noise on the acoustic reflex observed no significant change in average onset latency following a two-hour broadband noise (Rodriguez, Gerhardt, & Hepler, 1989). Zakrisson (1975) found unilateral Bell's palsy patients experienced a significantly greater threshold shift after exposure to a 500 Hz narrowband noise than in a state of normal stapedius reflex. This was not the case following a 2000 Hz narrowband noise that also elicited a TTS. In this experiment TTSs were unaffected by the stapedius paralysis.

The acoustic reflex latency has been a measure of interest in research with virtually no documentation of clinical use in differential diagnosis. According to Clemis and Sarno (1980a), the stapedius reflex latency “is broadly defined as the interval between the onset of an intense acoustic stimulus and the onset of the stapedius muscle contraction” (p. 603). It is also considered an indirect measure of neural conduction time (Clemis & Sarno, 1980b). The acoustic reflex latency is frequency dependent in terms of duration, variability, and magnitude, and is also intensity dependent. Clemis and Sarno (1980a) examined the acoustic reflex latency in adults with normal hearing sensitivity, cochlear lesions, and retrocochlear lesions. Results from this study support the notion that retrocochlear lesions involving the auditory nerve result in a prolongation of the reflex latency. Similarly, Jerger and Hayes (1983) examined acoustic reflex latency in subjects with confirmed acoustic neuromas. These researchers found that in ears with retrocochlear auditory nerve dysfunction the acoustic reflex latency showed a reduction in absolute amplitude as well as an alteration of reflex waveform morphologic features. They suggest that the previously mentioned prolonged latency measures for individuals with retrocochlear lesions may be an artifact of the interaction between the reduced amplitude and poor waveform morphology.

**Otoacoustic emissions.** OAEs were first described by David Kemp in 1978 and have been an area of interest ever since (Prieve & Fitzgerald, 2009). According to Kemp (2002), OAEs are the result of vibrations that occur as a “by-product of a unique and vulnerable cochlear mechanism which has become known as the ‘cochlear amplifier’ and which contributes greatly to the sensitivity and discrimination of hearing” (p. 223).

The “cochlear amplifier” refers to the nonlinear characteristics of cochlear responses and the exceptional sensitivity and frequency selectivity in the healthy cochlea. It is hypothesized that the cochlear amplifier enhances the vibration of the basilar membrane at the peak of the traveling wave and that this occurs particularly at low stimulus levels (Prieve & Fitzgerald, 2009). Evidence indicates that OHCs contribute to this boost in vibration. Numerous researchers have shown that when OHCs have been damaged or are missing, reduced auditory sensitivity, broader tuning, and abnormal response growth are observed. OAEs are a preneural phenomenon, an indirect measure of OHC function, and are vulnerable to acoustic trauma, hypoxia, and ototoxic medications. OAEs are relatively easy to record, quick to obtain in the clinical setting, and useful for corroborating audiometric data. A brief discussion on recording techniques and a comparison of TEOAEs and DPOAEs will follow.

OAEs are recorded by placing a small probe in the ear canal that houses one or two speakers as well as a microphone. The responses are very small and require signal averaging techniques. Each time the stimulus is presented, the resulting sound in the ear canal is sampled and synchronized with the eliciting stimulus. The stimulus is presented hundreds of times during the test and each response is averaged with the previously measured response (Prieve & Fitzgerald, 2009). The idea behind signal averaging is that the OAE response will be the same each time sampled and the noise and artifact will be random. The ultimate result will be an increase in signal-to-noise ratio as the noise will be reduced and the OAE response will be preserved. Due to the small nature of the responses, OAEs should be recorded in a sound attenuating booth

or quiet room. A good probe fit will help eliminate unwanted ambient or external noise (Kemp, 2002).

OAEs arise by two fundamentally different mechanisms: linear reflection or nonlinear distortion (Shera, 2004; Shera & Guinan, 1999). These two different mechanisms combine to form the emissions measured in the ear canal. Shera and Guinan (1999) have proposed a mechanism-based taxonomy to describe OAEs based on the mechanisms of their generation. SOAEs are emissions that arise solely by linear reflection and are due to “standing waves caused by multiple internal coherent reflection” (Shera, 2004, pg. 87). Reflection emissions also occur by linear reflections and are generated by backward-traveling waves arising through the linear reflection of forward-traveling waves. This occurs due to the pre-existing perturbations in the mechanics as seen with single frequency OAEs and TEOAEs measured at low levels. Distortion emissions, on the other hand, result from backward-traveling waves arising from sources induced by nonlinear distortion. These are primarily the result of cochlear nonlinearities, which act as sources of cochlear traveling waves (Shera & Guinan, 1999). Evoked emissions are typically a mixture of both mechanisms. It has been suggested that clinical measurement of both types of emissions will be needed to maximize the specificity of OAE testing as a noninvasive probe of cochlear function.

OAEs may also be classified by the means they are emitted: spontaneous and evoked by stimuli. SOAEs are measured in the absence of an eliciting stimulus and are considered evidence of an ‘active’ element of the cochlea (Prieve & Fitzgerald, 2009). Initially it was thought that SOAEs were an objective correlate of tinnitus. This was

found to only be the case in 1% to 9% of tinnitus cases. SOAEs are not used clinically at this time.

Evoked OAEs are measured in response to an eliciting stimulus. TEOAEs are recorded using time synchronous averaging and occur following the presentation of a transient or brief stimuli such as a toneburst or click. They can be evaluated in terms of level expressed in dB SPL, percent reproducibility, and signal-to-noise ratio. The TEOAE level varies with stimulus level in a nonlinear fashion, with linear growth at moderate stimulus levels and saturation occurring at higher levels of stimulation between 50 and 80 dB peak SPL.

DPOAEs are recording following the presentation of two pure tone stimuli, or primaries termed  $f_1$  and  $f_2$  with  $f_1$  lower in frequency than  $f_2$ . These primaries are also presented at two different levels, labeled L1 and L2. The concept of DPOAEs is that when the two primaries are close in frequency an interaction between them occurs on the basilar membrane resulting in an output of cochlear energy at other frequencies that are arithmetically related to the primary frequencies (Prieve & Fitzgerald, 2009). The largest level of DPOAE measured in humans occurs at  $2f_1 - f_2$  and, consequently, has been the most extensively studied. Maximal DPOAEs are also evoked when the primary relationship of  $f_2/f_1$  is equal to approximately 1.2. This has become a clinical standard. As conjectured, the level of the primaries can also affect measured DPOAE level. Normative data has suggested that the optimal L1-L2 separation when testing human DPOAEs should be calculated as  $L1 = 0.4(L2) + 39$  dB for the stimulus intensity range of 20 dB SPL to 65 dB SPL (Kummer, Janssen, & Arnold, 1998; Kummer et al., 2000).



DPOAE input/output (I/O) functions have been examined in normal hearing and hearing impaired humans (Dorn et al., 2001). According to Dorn et al. (2001), DPOAE I/O functions are linear at levels close to threshold, demonstrate compression for moderate levels, and show an additional linear pattern at high levels. Research has shown that DPOAE I/O functions can be measured over a wider range of levels in normal and hearing-impaired individuals (Dorn et al., 2001). DPOAE I/O function patterns were obtained in this study with  $f_2$  at half octave steps between 1000 Hz and 8000 Hz with L1 at 65 dB SPL or lower. Normal hearing ears exhibited a similar pattern for all frequencies except 8000 Hz. Normal hearing individuals seem to exhibit steep I/O functions at low and high stimulus levels with compression observed at moderate levels. Hearing impaired ears, on the other hand, exhibited steeper slopes and less compression over a reduced range of levels. DPOAE I/O functions seem to be measures of cochlear-response growth and changes in I/O functions can help describe the changes in cochlear response as a result of hearing loss in humans.

Kummer et al. (1998) studied the relationship between DPOAE I/O functions and auditory sensitivity as assessed by behavioral thresholds in humans. Participants were divided into two groups: normal hearing and moderate cochlear impairment. DPOAE I/O functions were found to be compressive in normal hearing subjects. That is, I/O functions exhibited strong saturation at moderate primary tone levels. In the hearing impaired ears, the reductions of DP level were greatest at lowest stimulus levels and smallest at highest stimulus levels resulting in a linearized DP I/O function. Kummer et al. (1998) suggest that due to these findings DPs should be measured at lower primary tone levels in addition to higher levels to aid in the prediction of the hearing threshold.

Lasky et al. (1994) examined the characteristics of DPOAE I/O functions from threshold to 65 dB SPL and how they vary as a function of frequency in humans. Eight normal hearing adults served as experimental subjects. The measurements were found to have impressive reproducibility within the same experimental session as well as when recordings were separated by more than four months. I/O functions can be described as “generally linear functions with slopes less than unity indicating compression of the [DPOAE] output as a function intensity of the input” (Lasky et al., 1994, p. 183). The slope of the functions does increase as a function of frequency.

### **Electrophysiological Auditory Assessment**

Auditory evoked responses are objective responses measured from the cochlea, auditory nerve, or auditory regions of the brain that are produced by an acoustic or auditory sound (Hall, 2007). These responses are recorded from electrodes placed on the scalp or in the ear and play an important role in the diagnosis of disorders of the ear, in intraoperative monitoring, and in diagnosis of central disturbances (Møller, 1994). Evoked potentials are small-amplitude, far-field responses that require sophisticated techniques to measure. Auditory evoked responses are categorized by the latency of the response with respect to the offset of the evoking stimulus. Early latency auditory evoked potentials are the main focus of this work and will be described in detail below. A short description of middle and late responses will follow as well.

**Early latency responses.** The early auditory evoked potentials consist of ECoChG and ABR responses. These responses are generated by the inner ear, auditory nerve, and auditory brainstem and occur within 10 ms of an eliciting brief transient stimulus. ECoChG and ABR have been used extensively in research studies

as well as in the clinical setting for the assessment of otology and neurologic impairment.

***Electrocochleography.*** ECoChG is a useful tool in the diagnosis, assessment, and monitoring of inner ear disorders and can be helpful in the diagnosis of retrocochlear disorders. It is thought to reflect the changes in anatomical position of hair cells and is a method of recording stimulus-induced potentials of the cochlea and typically occurs within 1.5 to 2 ms after an acoustic stimulus (Chung et al., 2004; Hall, 2007). The most common applications for ECoChG include diagnosing, assessment, and monitoring of Ménière's disease, enhancement of wave I of the ABR when hearing loss is present, and measurement and monitoring of auditory nerve function during surgery (Ferraro, 2000). ECoChG is a measurement of stimulus-related cochlear potentials and the response consists of three components: the CM, the SP, and the AP.

The CM can be recorded from anywhere within or on the cochlea or outside the cochlea on the promontory or external ear canal and is generated primarily by the outer hair cells of the basal turn of the cochlea (Hall, 2007). The CM is an alternating current that mirrors the waveform of the eliciting stimulus and can consequently be canceled from the response when an alternating polarity click is utilized. When a noninvasive recording montage is utilized it is often difficult to separate the CM from stimulus artifact (Ferraro, 2000). The utility of the CM in differential diagnosis in inner ear versus auditory nerve disorders has yet to be established (Ferraro & Durrant, 2006).

The SP is a direct current shift of the CM baseline representing the time-displacement of the cochlear partition in response to the stimulus envelope (Ferraro, 2000; Hall, 2007). This response is also generated primarily by the outer hair cells of

the cochlea and is typically seen as a downward deflection persisting for the duration of the acoustic stimulus (Ferraro & Durrant, 2006). The SP is quite a complex response and is thought to represent nonlinearities associated with the transduction process of the cochlea. It is clearly influenced by stimulus duration with little influence from stimulus frequency (Hall, 2007). The SP has been used commonly to aid in the diagnosis of Ménière's disease. The typical ECoChG finding for patients with Ménière's disease is an enlarged SP/AP amplitude ratio. Recently Ferraro (2010) suggested that the SP/AP area ratio has improved the sensitivity of ECoChG in the diagnosis of Ménière's disease while maintaining the high specificity.

The AP is a component of ECoChG as well as the ABR. According to Ferraro and Durrant (2006), it represents "the summed response of numerous, at times thousands of, auditory nerve fibers firing synchronously" (p. 48). It is a compound action potential that tends to be dominated by neural contributions of the basal end of the cochlea. The AP, like the CM, is an alternating current response and represents predominantly negative peaks as a result of the underlying neural firings. The AP is analogous to wave I of the ABR and arises from the distal portion of the auditory nerve. Clinically, most interest in the AP is focused on the latency and magnitude of the response. Unlike the CM and SP, the AP is a reflection of inner hair cell output. The AP response of ECoChG has been most extensively studied in assessment of cochlear and auditory nerve function, especially in surgical settings, and in the comparison of its magnitude to the magnitude of the SP in individuals suspected of having Ménière's disease.

Most commonly in the clinical setting an extratympanic electrode placement of either the external auditory canal or lateral surface of the TM is utilized. Transtympanic (TT) electrode placements are more commonly used in Europe but have not been well accepted in the United States (Ferraro, 2000). The TT approach is an invasive procedure where a needle electrode is passed through the TM and rests on the cochlear promontory or round window. The benefit of this recording approach is the increased signal-to-noise ratio due to the close proximity of the recording electrode to the generator. The negative of this approach, however, is that the invasive nature requires a physician to be present and puncturing the TM with a needle is quite painful even when anesthetic is utilized. For the extratympanic recording approach a recording electrode is either placed on the lateral surface of the TM or in the external auditory canal. This recording technique can be performed by an audiologist and is relatively painless. The down side to this technique is that more signal averaging is needed to obtain a response due to the distance from the generator being farther than with a TT approach. Ferraro (2010) recommends the lateral surface of the TM as the optimal noninvasive electrode site for ECoChG.

***Auditory Brainstem Response.*** The ABR is typically used for differential diagnosis and estimation of hearing threshold in difficult to test populations including infants and malingerers. It is best generated with very brief stimulus having an almost instantaneous onset, which enhances synchronous neural activity of many neurons (Hall, 2007). Click or tone burst stimuli are effective at eliciting the ABR and the response typically occurs within 10 ms after an eliciting stimulus. Similar to other

evoked potential responses, signal averaging is utilized to achieve an adequate signal-to-noise ratio to detect the small response within background electrical activity.

The ABR is recorded minimally with three electrodes. The electrode montage consists of one electrode located either at the top of the head or in the midline of the forehead, another near the ear on the stimulated side, and a ground electrode located anywhere (low forehead or contralateral ear; Hall, 2007). The response is influenced by several factors including but not limited to age, gender, body temperature, and hearing sensitivity.

The major peaks of the response are labeled by roman numerals, as in wave I through wave V. Each wave has its own respective generator. Waves I and II are both generated by the auditory nerve. More specifically, wave I is generated by the distal (lateral) portion of the auditory nerve and wave II is generated by the proximal (medial) portion of the auditory nerve (Musiek & Baran, 1986). Wave III most likely has multiple generator sites with the most prominent being the CN. Wave IV also has multiple generators with the primary response coming from the SOC with a stronger contralateral contribution than ipsilateral. Finally, wave V is generated by the LL. This is an oversimplification of the anatomy behind the ABR. The ABR, as mentioned previously, is a response to synchronous discharges of the auditory nerve and brainstem pathway. It is understood that the stimulated neural fibers may come from a variety of different structures in the brainstem (Musiek & Baran, 1986).

The ABR is used frequently in the clinical setting. One benefit of the ABR is the ability to obtain frequency specific information in young children and infants. The automated ABR is utilized in newborn hearing screenings for infants prior to discharge

from the hospital. Neurodiagnostic testing of auditory nerve and brainstem dysfunction can be completed with use of the ABR. Intraoperative monitoring of eighth nerve and auditory brainstem status during surgery and the differential diagnosis of auditory neuropathy have also been attributed to the ABR (Hall, 2007). Unfortunately, the ABR is not a test of hearing and cannot provide information on auditory function above the brainstem. The click stimulus is also poor at estimating hearing sensitivity outside the 1000 Hz to 4000 Hz region.

**Middle latency responses.** The MLR occurs between approximately 12 ms and 80 ms, shortly after the ABR and before the auditory late response. The typical electrode array consists of a noninverting electrode on the scalp or side of the head midway between the ear and vertex with inverting electrode near the ear (Hall, 2007). This response is thought to reflect synchronous firing of auditory neurons in thalamocortical pathways including both subcortical and cortical auditory structures (Al-Saif, Abdeltawwab, & Khamis, 2012; Weihing, Schochat, & Musiek, 2012). The waveform of the MLR appears as positive (P) and negative (N) sequences identified as Po, Na, Pa, Nb, Pb, and Nc. Na, Pa, Nb, and Pb have increased amplitude and consistency and, as a result, are the components of the MLR most often evaluated. It is thought that the Pa component of the response is generated in the auditory thalamus and primary auditory cortex while the Pb component is produced by activity in the secondary auditory regions (Hall, 2007).

The MLR is most often evoked by click stimuli with a sharp onset; however, tonal stimuli with relatively long duration are more effective at eliciting the response (Al-Saif et al., 2012; Hall, 2007). The MLR is less related to state of arousal than any other cortical

evoked potential; however, it cannot be reliably recorded from younger children under sedation or in some sleep stages (Hall, 2007; Weihing et al., 2012). It is advantageous over other evoked potentials as it has a robust morphology at even low intensity levels and has good morphology to pure tone stimuli (Weihing et al., 2012). A disadvantage of the MLR is that it can be confounded by muscle artifact and movement interference.

Numerous clinical applications for the MLR have been identified. The MLR has been valuable in detecting auditory central nervous system dysfunction including auditory processing disorders above the level of the brainstem as well as in estimating frequency specific auditory sensitivity in older children and adults (Hall, 2007). A few caveats to MLR testing should be noted including that the MLR response is not adult-like until approximately 10 years of age and that the response is significantly affected by anesthetic agents and central nervous system suppressants.

**Long latency responses.** Auditory late responses (ALRs) occur between 50 ms and 500 ms and are much larger and lower in frequency than early and MLRs (Hall, 2007; Kraus & Nicol, 2009). Due to the fact that these responses differ dramatically in morphology and timing and overlap one another, they are categorized into two broad groups: exogenous or endogenous. Auditory evoked response discussed to this point including ECoChG, ABR, and MLR are exogenous responses. Exogenous responses are obligatory responses to sound requiring no active participation from the listener to obtain optimal response and are dependent directly on stimulus characteristics. They typically occur within the first 250 ms following the eliciting stimulus (Surwillo, 1980). Endogenous responses, on the other hand, depend on events internal to the nervous



system including the subject's attention, expectations, and decisions, and require stimulus manipulation or the performance of a task by the patient (Kraus & Nicol, 2009).

The P1-N1-P2 complex is exogenous in nature. This response contains a positive going peak P1 (sometimes classified as a MLR) at approximately 50 ms to 80 ms, the first negative going peak N1 between 100 ms and 150 ms, the second positive going peak P2 occurring at approximately 150 ms to 200 ms, and a negative going peak N2 between 180 ms to 250 ms (Hall, 2007). These responses are all cortical in nature arising from the primary auditory cortex and auditory association areas of the temporal lobe and do not mature until post adolescence (Kraus & Nicol, 2009). The P1-N1-P2 complex is used clinically to assess the higher level auditory central nervous system functioning and auditory processing, assessment of cognitive functioning in individuals with neuropsychiatric disorders, and for documentation of auditory training benefits (Hall, 2007).

The MMN and P300 responses are both considered endogenous responses. Endogenous, meaning 'born within', responses arise due to some level of cognitive processing (Kraus & Nicol, 2009). The MMN response bridges the gap between exogenous and endogenous auditory evoked potentials. MMN does not require attention; however, it is elicited by a discriminable change in a sequence of otherwise identical repeating stimuli. The paradigm eliciting this response is called an "oddball paradigm" where a target, or deviant, is placed within a series of frequent stimuli. The deviant can differ in intensity, frequency, or complexity and can be at or below perceptual threshold (Kraus & Nicol, 2009). The response to the infrequent stimulus differs to that of the frequency stimulus and creates a slow negative deflection between

150 ms and 300 ms from change onset and is most noticeable when waveform for the standard stimulus is subtracted from the waveform of the infrequent stimulus. (Hall, 2007; Kraus & Nicol, 2009). This waveform is termed the “difference wave”. Extensive research has produced evidence suggesting the generator of MMN to be in the auditory cortex of the temporal lobe and the frontal lobe, as well as from subcortical areas (Hall, 2007). Advantages of MMN include that it is attention-independent in its elicitation, may be elicited in sleep or coma, and can be an objective measure for the temporal window of integration in auditory processing (Näätänen & Excerpta, 2000).

The P300, an endogenous response, also utilizes an oddball paradigm; however, this evoked potential requires the listener consciously attend to the deviant stimulus. This response is considered an index of cognition due to the fact that the listener must evaluate and classify the stimuli (Kraus & Nicol, 2009). Human depth electrode studies have provided evidence that the P300 is generated in multiple auditory sub-cortical areas including the hippocampus of the medial temporal lobe region and possible thalamic contributions (Hall, 2007). The response is a large positive peak of approximately 5 microvolts ( $\mu\text{V}$ ), labeled P3, occurring at approximately 300 ms following a deviant auditory stimulus. The P300 is advantageous in the clinical setting as it can assess higher levels of auditory processing and document the effectiveness of medical and nonmedical management for different disorders including but not limited to attention deficit hyperactivity disorder and central auditory processing disorder. The biggest disadvantage to this test is the marked effect of minor alterations in attention on the response (Hall, 2007).

## **Audiometric Profile of Normal Hearing**

In order to appropriately describe the audiometric profile of NIHL one must define normal hearing for young adults. Pure tone testing is the most common measure of normal hearing sensitivity. The criteria for normal hearing differ among different sources. As described previously, Goodman (1965) presented the most commonly utilized criteria. Normal hearing sensitivity for a normal hearing young adult is described as air conduction thresholds to pure tone stimuli better than or equal to 25 dB HL at octave and inter-octave frequencies between 250 Hz and 8000 Hz.

Tympanometric measures are essential for evaluating middle ear function. As discussed previously, tympanometric indices include ear canal volume, peak compensated static acoustic admittance, tympanometric peak pressure, and tympanometric width. These indices are useful in identifying pathology of the middle ear system. Roup et al. (1998) evaluated normative tympanometric data for normal hearing young adults ranging in age between 20 and 30 years. These norms are gender specific with males having significantly larger ear canal volume and peak compensated static acoustic admittance and smaller tympanometric width than females. The gender combined norms are as follows: 0.30 - 1.50 mmhos  $Y_{tm}$ , 0.90 cm<sup>3</sup> - 1.80 cm<sup>3</sup>  $V_{ea}$ , and 35.80 daPa - 95.00 daPa TW.

As discussed previously, the greatest amplitude and most robust DPOAE measured in humans occurs at  $2f_1 - f_2$  and, consequently, has been the most extensively studied. Maximal DPOAEs are also evoked when the primary relationship of  $f_2/f_1$  is equal to approximately 1.2. This has become a clinical standard. Primary tone level separation of either a 15- or 10-dB level separation ( $L_1 > L_2$ ) produces the largest

DPOAE amplitude in normal hearing adults (Abdala, 1996). The DPOAE response pattern as a function of frequency is a nonlinear relationship with two maxima (at 1440 and 4561 Hz) and a dip (at 2873 Hz) in the DP-gram. Generally speaking, the higher the primary frequencies the higher the response amplitude (Vinck et al., 1996).

According to Gorga et al. (2005), DPOAE response signal to noise ratio and DPOAE absolute level should be considered in determining normal DPOAE responses. Normal responses are based on a cumulative distribution of responses from both normal and impaired ears with predetermined hit rates and false-alarm rates. Typically, DPOAE signal to noise ratios should be greater than or equal to 6 dB to be considered present. In some instances, the noise floor can be high enough that the absolute DPOAE responses are not greater than or equal to 6 dB above the noise floor. In this case Gorga et al. (2005) recommends that results would be uninterpretable because the large DPOAE responses could be nothing more than noise. Similarly, signal to noise ratios may be positive and greater than 6 dB while DPOAE absolute values are low. In this case the results cannot be assigned to normal or impaired distribution. Inevitably some interpretations will be wrong due to the predetermined false-alarm rate for the cumulative distribution. A good rule of thumb for the lower limit of normal absolute amplitude in normal hearing young adults is 0 dB SPL (Dhar & Hall, 2012).

ECochG is a measure of stimulus-related cochlear potentials and has most often been utilized to diagnose, assess, and monitor Ménière's disease, for enhancement of wave I of the ABR, and to measure and monitor cochlear and auditory nerve function during surgery involving the auditory periphery (Ferraro, 2000). ECochG responses are dependent upon the recording techniques including recording site, recording

parameters, and specific stimulus considerations. It is well known that recordings using an electrode on the lateral surface of the TM yield larger amplitudes than TIPtrode™ recordings; however, larger variations in the SP/AP amplitude ratios are also noted (Park & Ferraro, 1999).

Normal ECoChG responses include the CM, SP, and AP. The CM and the SP are predominately generated by the outer hair cells of the organ of Corti. The CM effectiveness in differential diagnosis of inner ear disorders is not yet known and, consequently, is often inhibited by using a stimuli presented in alternating polarity. The SP is a direct current potential that is dependent on the duration of the stimulus and is often enlarged in patients with Ménière's disease. The AP, on the other hand, is an alternating current potential representing the synchronous firing of thousands of auditory nerve fibers. The most useful AP features include its latency and magnitude. ECoChG is currently the only method of detecting increased inner ear pressure; however, there is a lack of reliable ECoChG normative data, which is most likely attributed to the lack of universal standards and the vulnerability to operator bias. Normative data for recordings on the lateral surface of the TM to 88 dB nHL clicks of alternating polarity in normal hearing young adults include: mean AP amplitude of 1.30  $\mu$ V; mean AP latency of 2.25 ms; mean SP/AP amplitude ratio of 0.31  $\mu$ V; and mean SP amplitude of -0.29  $\mu$ V (Levine et al., 1992).

### **Audiometric Profile of Noise-Induced Hearing Loss**

NIHL is a public health problem with an estimated 10% of the world exposed to sound pressure levels that could potentially cause NIHL and approximately half of those individuals experiencing hearing loss as a result of noise exposure (Basner et al., 2014).

Excessive noise exposure can result in three types of hearing changes: noise induced TTS, noise induced PTS, and acoustic trauma (Feuerstein & Chasin, 2009). A noise induced TTS is often characterized by reduction in hearing sensitivity, a sensation of aural fullness due to the reduction in high-frequency hearing sensitivity, and tinnitus, or ringing in the ears. The amount and duration of the noise induced TTS is dependent upon the duration and intensity of the noise. Typically, within a few hours to a few days thresholds will return to normal. Noise induced PTS is similar to noise induced TTS except there is less than a full recovery of the pre-exposure threshold (Feuerstein & Chasin, 2009). Duration, intensity, and spectrum of the noise all contribute to the noise induced PTS. Acoustic trauma, on the other hand, often occurs following a brief exposure to a very intense sound such as an explosion. This results in permanent cochlear damage, possible TM or ossicular chain damage, and immediately noticeable hearing loss.

The challenge in diagnosing NIHL is that there are copious contributors to hearing loss, one of the most prevalent being age related hearing loss. Coles, Lutman, and Buffin (2000) set out to assist in the diagnosis of NIHL to distinguish between the possibility and probability of NIHL for legal purposes. It is easy to identify an individual with NIHL if they have a history of unprotected high intensity and long duration noise exposure and the audiogram reveals a classic notch at 3000 Hz, 4000 Hz, or 6000 Hz. This, however, can often be obscured by age-associated hearing loss as well as other factors including but not limited to hereditary factors and use of ototoxic medications (Coles et al., 2000). Coles et al. (2000) determined that the only criterion on which to base the decision that noise has made a material contribution to an individual's hearing

impairment is “the presence of a degree of noise-induced hearing loss that is large enough to be measurable reliably and identifiable on the audiogram” (p.264). The guidelines set forth to diagnose NIHL consist of three requirements. The first requirement is that a high frequency hearing loss must be identified at 3000 Hz, 4000 Hz or 6000 Hz that is 10 dB or greater than the hearing threshold levels at 1000 Hz or 2000 Hz. The second requirement set forth in these guidelines is split into two categories and the patient must meet one of the two requirements. The noise exposure reported must have been (a) daily eight-hour continuous exposure of at least 85 dB(A) for a sufficient number of years to lead to a cumulative exposure of 100 dB(A) Noise Immission Level or (b) daily eight-hour continuous exposure of at least 85 dB(A) leading to a total Noise Immission Level of 90 dB(A) to account for those more susceptible to NIHL. If (a) has been met then the third requirement is that the audiometric configuration be a downward notch within the 3000 Hz to 6000 Hz range or a sufficiently large relative bulge downwards and to the left in the 3000 Hz to 6000 Hz range. This bulge is typically the result of age associated hearing loss, which causes the high frequency notch to be missing. If (b), on the other hand, has been met, then the third criteria is similar to the previous except that the bulge must be at least 20 dB to qualify.

The American College of Occupational and Environmental Medicine (ACOEM) reports that NIHL is one of the most prevalent occupational conditions (ACOEM, 2003). This can be attributed in part to the fact that excessive noise is pervasive in a wide range of industries. Typically, NIHL develops gradually over a number of years as the result of either continuous or intermittent loud noise exposure. NIHL is typically sensorineural in nature affecting hair cells of the inner ear and most often occurs

bilaterally. The first sign is the classic notching of the audiogram between 3000 Hz and 6000 Hz with some degree of recovery at 8000 Hz (ACOEM, 2003; Dobie, 2005). The exact positioning of the notch is dependent upon factors including the frequency of the noise and the length of the ear canal. Most often NIHL does not produce thresholds of greater than 75 dB in the high frequencies and 40 dB in the lower frequencies (ACOEM, 2003). NIHL can, however, be superimposed on age associated hearing loss with the result being thresholds poorer than the above-mentioned. Interestingly, the rate of loss due to noise exposure is the greatest in the first 10 to 15 years of exposure and decreases as hearing thresholds increase (ACOEM, 2003).

OAEs provide objective information on the integrity of outer hair cell function and have been suggested to be particularly useful for assessing damage due to noise overexposure (Marshall & Heller, 1998). OAEs are known to reflect the mechanical nonlinearity of the cochlea and are also physiologically vulnerable to ototoxic exposure including but not limited to noise exposure (Engdahl & Kemp, 1996). Changes due to moderate noise exposure resulting in TTSs have also been shown to alter the amplitude or frequency composition of TEOAEs, DPOAEs, and SOAEs (Barros et al., 2007; Engdahl & Kemp, 1996; Lapsley-Miller et al., 2006; Marshall & Heller, 1998; Montoya et al. 2008; Olszewski et al., 2005; Reuter, Ordoñez, & Hammershøi, 2007; Shupak et al., 2007; Sisto et al., 2007; Vinck et al., 1999). Findings on this matter are equivocal. The following will be a review of the effects of noise exposure on TEOAEs and DPOAEs in humans.

Marshall and Heller (1998) examined the effect of noise exposure on TEOAEs in hopes of using this test as a measure of noise-induced threshold shift. TEOAE and



behavioral threshold measurements were made in humans before and after exposure to 10 minutes of a 105 dB SPL half octave band noise centered at 1414 Hz. They found that the maximum temporary emission shifts were half to one octave above the noise exposure frequency and the average temporary emission shift of 4.7 dB was less than half of the 11.7 dB average TTS. It was also found that the average recovery times for emissions and thresholds were similar and “the average TTS magnitude along the recovery function was predictable from [temporary emission shift] magnitude” (Marshall & Heller, 1998, p. 1319). This study concluded that both TEOAEs and behavioral thresholds reveal the same aspects of inner ear changes following noise exposure.

Barros et al. (2007) also investigated the role of pure tone audiometry and TEOAEs in detecting subtle temporary changes following noise exposure. Thirty young adults employed in a textile factory for at least one year and not more than three years were exposed to elevated sound pressures levels of around 80 to 90 dB SPL. Pure tone threshold and TEOAE measurements were made before and after five hours of exposure to elevated sound pressure levels. TEOAEs were measured at 1000, 2000, 3000, and 4000 Hz. Pure tone audiometry results showed threshold shifts at all frequencies tested with the most significant shifts being 4000 Hz in the right ear and 3000 Hz in the left ear. Statistically significant differences ( $p < .05$ ) were found at all frequencies for both ears when comparing responses before and after exposure. Following exposure to elevated sound pressure levels TEOAE results revealed reduced reproducibility at all frequencies for both ears. The most significant reproducibility changes were seen at 1000 Hz for both the right and left ears. Barros et al. (2007) found that TEOAEs had a role in detecting significant changes in reproducibility of

TEOAE responses (reduced reproducibility from 1000 Hz to 4000 Hz) after exposure to five hours of high sound pressure levels.

Olszewski et al. (2005) examined the specific effects of short-term impulse noise on TEOAE responses of 80 healthy subjects. Half of these subjects were male recruit soldiers with shooting training and the other half were young male controls. All subjects had normal hearing with thresholds between 10 and 15 dB. TEOAEs were obtained three to five minutes prior to shooting and then at two minute intervals one, two, and three hours post-exposure. The same paradigm was utilized with the control group. TEOAE shifts in amplitude were maximum at 4000 and 5000 Hz and minimum at 1000 and 2000 Hz following impulse noise generated by rifle gunshots. The recovery time was also prolonged if the TEOAE magnitude reduction was higher.

The effect of noise exposure on DPOAEs has also been of great interest. Engdahl and Kemp (1996) specifically evaluated the vulnerability to noise exposure of five different DPOAE paradigms: across a wideband of frequency, microstructure, input/output function, primary frequency ratio tuning curve, and group delay. In this study nine subjects with normal hearing were exposed to a 2000 Hz narrowband noise with third octave bandwidth at 102 +/- 2 dB SPL for 10 minutes. The initial measurements were made and were then followed by the noise exposure and repeated DPOAE measurements were obtained in the first 33 minutes following exposure. When examining the effects of the noise exposure on the DPOAE response during a low-resolution wideband sweep the greatest effect was in the 3000 Hz to 5000 Hz region with a relatively smooth recovery. This effect was greatest at approximately one half octave above the noise exposure. According to Engdahl and Kemp (1996), "the

maximum to minimum ratio of the DPOAE microstructure decreased and the whole pattern shifted toward lower frequency after the noise exposure” (p. 1586). It was also noted that the greatest amplitude reduction following noise exposure was at low primary levels, similar to a previous study showing that DPOAE amplitudes are most vulnerable at low levels after aspirin consumption in humans (Wier, Pasanen, & McFadden, 1988). As a result of the high sensitivity of low levels to noise exposure, the use of these low level DPOAEs was considered a safe and sensitive monitor of susceptibility to noise.

Reuter et al. (2007) investigated the effects of a 1000 Hz tone lasting three minutes at 105.5 dB SPL on properties of DPOAEs including broadband DPOAE and the DPOAE fine structure. Broadband DPOAE responses and DPOAE fine structure were measured in normal hearing young adults. The post exposure measurements were taken every two minutes starting at one-minute post exposure for the first group and one minute and forty seconds for the second group. The last three measurements were then taken every five minutes starting at ten minutes for group one and twelve minutes and twenty seconds for group two. This study found that the amount of TTS was higher in the early recovery time period but similar to DPOAE shift at later recovery times and the maximum shift for DPOAEs and thresholds occurs in a frequency range above the exposure frequency supporting the idea of the spread of excitation towards the basal end of the cochlea with increases in exposure level.

Wooles et al. (2015) examined whether DPOAEs can serve as a replacement for pure tone audiometry for screening of occupational noise exposure related auditory deficits. Sixteen male brickyard workers ranging in age from 20 to 65 years served as participants. Pure tone thresholds and DPOAEs were obtained over the course of one

day during a routine screening. Results from this study revealed that DPOAEs are not a suitable replacement for pure tone audiometry in clinical practice. DPOAE amplitudes and pure tone audiometric thresholds exhibit poor correlation, which does not support their use to predict hearing thresholds clinically.

Some researchers have examined the effects of noise exposure on both TEOAEs and DPOAEs (Lapsley-Miller et al., 2006; Shupak et al., 2007; Sisto et al., 2007; Vinck et al., 1999). Lapsley-Miller et al. (2006) measured TEOAEs and DPOAEs in 338 sailors with normal thresholds and middle ear function before and after six months of exposure to aircraft carrier noise. This study found that the average amplitudes of OAEs decreased significantly while there were no statistically significant changes in audiometric thresholds. There were no statistically significant correlations in changes of audiometric thresholds and changes in OAE amplitudes. The changes in TEOAE amplitudes and DPOAE amplitudes were moderately correlated. There were only 18 ears that exhibited a PTS and only one-third of these ears showed significant OAE shifts that mirrored the PTS. The best predictor of PTS was TEOAE amplitude in the 4,000 Hz half-octave frequency band. Lapsley-Miller et al. (2006) suggested that it is possible the OAEs indicate noise-induced changes in the inner ear that are undetected in audiometric testing and, as a result, may be a diagnostic predictor for NIHL risk.

Montoya et al. (2008) evaluated the effects of MP3 player noise on TEOAEs and DPOAEs in 40 ears of normal hearing young adults. TEOAE and DPOAE incidence, amplitude, and spectral content were analyzed in individuals with over two years of reported MP3 player noise. These participants were then divided into two categories:

those with moderate exposure (one hour to less than six hours per week) and those with heavy exposure (greater than six hours per week). Subjects were also classified into three additional groups according to MP3 player use: less than five years, between five and ten years, and greater than ten years. The amplitude levels of noise exposure were not evaluated in this study. This data was compared to a control group comprised of 232 ears with no MP3 noise exposure. A reduction in TEOAE and DPOAE incidence and amplitude as well as an increase in DPOAE threshold were identified in subjects with the most MP3 player use to include most years and more hours per week of use. Montoya et al. (2008) also found that TEOAEs showed statistically significant lower incidence and amplitudes for normal hearing subjects with MP3 player use, especially at 2000, 3000, and 4000 Hz. As for DPOAE findings, incidence was lower at 700, 1000, 1500, and 2000 Hz; amplitudes were lower between 1500 and 6000 Hz; and thresholds were significantly higher from 1500 to 6000 Hz. Montoya et al. (2008) suggest that the cochlear impairment as a result of MP3 player noise may be detectable in OAE measurements prior to changes in other clinical tools.

Shupak et al. (2007) investigated the longitudinal effects of daily occupational noise ranging from 87 to 117 dBA on DPOAEs and TEOAEs in normal hearing male ship engine recruits and a control group with no noise exposure. The post exposure hearing evaluation occurred at least 48 hours following the last exposure time to rule out any effects of TTS. TEOAE amplitudes, DPOAE amplitudes, and contralateral suppression of TEOAEs were obtained. Shupak et al. (2007) suggested that the DP-gram is not significantly correlated with the pure tone audiogram and, as a result, should not be used as an objective measure of pure tone thresholds in early NIHL. TEOAEs,

on the other hand, did show high sensitivity in predicting NIHL, however, cannot be used as an efficient screening tool due to the high false-positive rates where TEOAE amplitudes were decreased with normal auditory thresholds after two years of noise exposure. MOC reflex strength, as assessed with suppression of TEOAEs, had no relation to individual vulnerability to NIHL.

Sisto et al. (2007) examined the longitudinal effects of noise exposure on TEOAEs and DPOAEs. Specifically, this study investigated the correlation between TEOAE signal to noise ratio and DPOAE level with one-third octave resolution and the audiometric threshold. Measurements were performed on young adults with different levels of exposure to industrial noise. It was determined that “if both OAE data and audiometric data are averaged over a significantly large bandwidth, the correlation between DPOAE levels and audiometric hearing threshold is sufficient to design OAE-based diagnostic tests with good sensitivity and specificity in a very mild hearing loss range, between 10 and 20 dB” (Sisto et al., 2007, p. 387).

Vinck et al. (1999) evaluated the sensitivity and applicability of TEOAEs and DPOAEs as measurements of the functional integrity of OHCs following TTSSs. Both artificial and natural tests of auditory fatigue were utilized to examine the sensitivity of OAEs in noise exposure. In the first experiment ten normal hearing young adults were exposed to one hour of broadband white noise at 90 dB SPL. The second experiment, on the other hand, consisted of five consecutive hours of discotheque music. Both experiments consisted of three pre-exposure measures averaged to serve as the pre-exposure baseline. Post exposure measures differed slightly between experiments. In the artificial noise exposure experiment TEOAE and DPOAE measures were obtained

during quiet breaks at ten-minute intervals throughout the one-hour exposure period and post-exposure measures were obtained over the course of 60 minutes at four-minute intervals. No measurements were obtained during exposure for the natural exposure experiment. Following the five-hour exposure, TEOAEs, DPOAEs, and audiometric thresholds were obtained at 25-minute intervals for the eight-hour recovery interval.

After exposure to the artificial noise TEOAEs exhibited a decrease in amplitude when compared to the pre-exposure baseline. Specifically, a statistically significant 20% reduction of the emission levels was identified when compared to the baseline. TEOAE results also showed the greatest sensitivity to noise exposure for the 4000 Hz band with both reproducibility scores and signal-to-noise ratio values. DPOAE results showed a significant reduction in amplitude of the response in the frequency region from 2793 Hz to 5582 Hz with frequencies below this range remaining unchanged. In the artificial noise exposure experiment DPOAEs were more sensitive to TTSS in describing the time course of recovery when compared to behavioral thresholds.

Following exposure to the discotheque music TEOAE mean group total response was significantly reduced from 12.22 dB SPL to 5.65 dB SPL at the first post-exposure measurement. After the complete eight-hour recovery period the response level had not fully recovered. The most substantial changes in reproducibility and signal-to-noise ratios were observed in the 4000 Hz frequency band. The band reproducibility score was reduced by 20.50% without recovering within the recovery phase. This pattern was also observed for signal-to-noise ratio values. These TEOAE results illustrate the high sensitivity for measuring the reaction of OHCs following noise exposure, especially at

4000 Hz. DPOAE results also showed high sensitivity in monitoring the effects of intense noise exposure. Significant mean amplitude reductions were observed in the frequency region between 3049 Hz and 5582 Hz. This range corresponds well to the observed 4000 Hz to 6000 Hz dip observed in the pure tone audiogram following noise exposure.

The TEOAE and DPOAE results from both of the Vinck et al. (1999) experiments illustrate that there are peri- and post-stimulatory effects on OHC function following intense noise exposure. Specifically, TEOAE and DPOAE responses were significantly reduced and did not fully recover in the 4000 Hz frequency range even though the pure tone audiogram did not show hearing loss. This suggests that OAEs are more sensitive than the behavioral audiogram in detecting subtle changes in OHC function.

The relationship between auditory threshold and DPOAE I/O functions has been studied extensively in animals (Eddins, Zuskov, & Salvi, 1999; Froymovich et al., 1995) and humans (Dorn et al., 2001; Engdahl & Kemp, 1996; Kummer et al., 1998; Lasky, Snodgrass, & Hecox, 1994). DPOAE I/O functions in most species consist of two components, one elicited at low stimulus levels and the other elicited at high stimulus levels. DPOAEs elicited at low stimulus levels are reduced or eliminated when the hair cells are damaged while DPOAEs elicited at high stimulus levels remain relatively resistant to cochlear damage. In hopes of examining the extent to which the DPOAE recovers after acoustic overstimulation, Froymovich et al. (1995) exposed six white, leghorn chickens to a 1500 Hz pure tone presented at 120 dB SPL for 48 hours. Immediately following exposure all thresholds on the DPOAE I/O functions were shifted to the right near the detection threshold at all frequencies meaning that the thresholds



occurred at a higher level of  $f_1$  and  $f_2$ . The greatest effect occurred at and above the exposure frequency. The high level component of the I/O function, on the other hand, showed a statistically significant increase in slope at or above the exposure frequency. As a result, DPOAE responses obtained at the highest stimulus levels were equal to or greater than normal. Interestingly, the I/O functions at the highest and lowest frequencies returned to normal after an eight-week recovery period while the I/O functions near the exposure frequency showed almost no improvement during the same recovery period.

Eddins et al. (1999) examined the reduction in DPOAE amplitude resulting from prolonged noise exposure. In this study, five chinchillas exposed to an octave-band noise centered at 4000 Hz for a total of 42 days with each six-day period at seven different intensity levels ranging in eight dB steps from 48 to 96 dB SPL. The DPOAE growth functions were then measured at octave intervals over a range of primary tone  $f_2$  frequencies between 1200 and 9600 Hz. This continuous noise exposure was found to cause the greatest reduction in DPOAE amplitude at  $f_2$  frequencies at or above the 4000 Hz octave-band noise exposure. It was also observed that by increasing the level of the noise in a stepwise manner, systematic changes in DPOAE I/O functions were produced. Initially it was noted that a minimal level of 50 dB SPL was needed to cause a change in DPOAE amplitude. The greatest amplitude reduction was observed for approximately a half-octave above the 4000 Hz octave-band noise. The DPOAE amplitude loss did increase with exposure up to 72 dB SPL with little or no additional reduction observed at levels above 72 dB SPL. The DPOAE amplitude decrease observed for exposure levels between 50 dB SPL and approximately 72 dB SPL was

1.3 dB for every dB increase in noise level.

Engdahl and Kemp (1996) examined the effect of a 102 dB  $\pm$  2 dB narrowband noise centered at 2000 Hz with a third-octave bandwidth on DPOAE I/O functions in normal hearing young adults. These researchers noted that the greatest sensitivity to noise exposure was obtained for low primary levels where DPOAE amplitude reduction was maximum. Similar to the Eddins et al. (1999) study in chinchillas, Engdahl and Kemp (1996) also found that the greatest reduction in DPOAEs occurs at approximately half an octave above the frequency of the noise exposure.

Effects from noise exposure have also been examined in ECoChG responses. Based on the fact that the intra- and inter-test reliability of ECoChG is good allowing for the detection of a real change in cochlear electrophysiology, Nam and Won (2004) predicted that ECoChG could detect the subtle changes in HC function due to TTS. They postulated that ECoChG would be a useful screening tool and can also be used in monitoring of NIHL. Participants in this study included 10 normal hearing young adults exposed to three consecutive hours of computer-game arcade noise. The intensity and frequency of the noise were determined by 10 minutes of measurements over the entire exposure period. Pure tone audiometry and ECoChG were performed before exposure, within 30 minutes of exposure, and 24 hours after exposure. The amplitudes of the SP and AP as well as the SP/AP amplitude ratio were measured. Noise analysis evidenced levels from 90.3 to 105.3 (91.5  $\pm$  4.5) dB SPL and consisted of primarily broadband noise composed of frequencies below 1000 Hz. Statistically significant ( $p < .05$ ) threshold shifts as assessed with behavioral audiometry were measured at all frequencies tested immediately post-exposure but did remain in the normal range. At

24 hours post-exposure the recovery period was significant at all frequencies with thresholds returning to pre-exposure levels. When compared to pre-exposure values, the SP and the SP/AP ratio increased significantly immediately following exposure while the AP did not change significantly. It was noted that there was no statistically significant change in the AP any time before or after the exposure. Since the SP/AP ratio exceeded the normal limit following noise exposure but the four-frequency pure tone average thresholds did not, Nam and Won (2004) believed that the SP/AP amplitude ratio is a more sensitive measure of noise-induced cochlear change than TTSs and that an elevated SP/AP amplitude ratio indicates temporary, reversible damage.

Kim et al. (2005) investigated the sensitivity and specificity of not only ECoChG but DPOAEs as well in determining the earliest noise-induced damage to the cochlea. Twenty normal hearing young adults volunteered for this study. Participants were exposed to two consecutive hours of music in the same nightclub. The 15-minute noise analysis indicated that the broadband noise had a peak between 1000 and 2000 Hz with intensity of  $90.3 \pm 4.2$  dB SPL. Pure tone audiometry, DPOAE, and ECoChG measurements were made pre-exposure, within 60 minutes of exposure, and 24 hours post-exposure. The observed threshold shifts as well as recovery from the shifts were statistically significant at all frequencies tested. The DPOAE absolute amplitude changes were statistically significant at all frequencies tested with the largest reduction occurring at 2000 Hz. When 24 hour post-exposure values were obtained a complete recovery had occurred. Statistically significant decreases in DPOAE SNRs were measured at 2000, 3000, and 4000 Hz. ECoChG results also showed statistically

significant changes to include an increased SP and an increased SP/AP ratio during the TTS phase. The AP duration also increased significantly while the AP amplitude did not change. The SP amplitude, SP/AP amplitude ratio, and the AP duration all returned to pre-exposure values and no change was noted in the AP amplitude at any observation time. The degree of correlation between pure tone thresholds and both DPOAE SNRs and ECoChG measurements were analyzed as well. Statistically significant inverse correlations between pure tone thresholds and DPOAE SNRs were identified with the correlation being more negative at higher frequencies. Statistically significant correlations were also identified between the six-frequency pure tone average and the SP amplitude, SP/AP amplitude ratio, and the AP duration. More specifically, the SP/AP amplitude ratio and pure tone average results were correlated at every frequency. There was no statistically significant correlation observed between pure tone average results and AP amplitude. It was noted that the shape of the electrocochleogram changed gradually with the TTS in that the AP became more obtuse and wider and the location of the SP fell. Kim et al. (2005) concluded that DPOAEs are not the most sensitive test for detecting OHC damage. They determined that, based on the results of this study, ECoChG is useful for early detection of NIHL between the TTS stage and mild hearing loss. This compares to DPOAE data in that DPOAEs are more sensitive to damage in the mild and permanent hearing loss range. Finally, it was determined in this study that ECoChG is more sensitive and specific than DPOAE indices for detecting a noise-induced TTS. As a result, Kim and colleagues proposed that ECoChG is useful in evaluating agents that protect against NIHL.

## **Management of Noise**

Excessive and potentially harmful noise exposure affects over 30 million American workers and is considered the most common occupational and environmental hazard with an estimated \$242 million spent on compensation for hearing loss disability (Rabinowitz, 2000; Basner et al., 2014). In 1956, the first regulations on noise exposure were introduced for personnel in the United States Air Force (Feuerstein & Chasin, 2009). Since that time there have been advances in the regulations of noise exposure including monitoring requirements of auditory thresholds and hearing conservation programs in both the United States and internationally.

Noise exposure can have nonauditory effects in addition to the acoustic trauma previously discussed. These nonauditory effects of noise exposure include effects on the cardiovascular system, sleep, fetal development, and cognitive performance in children. According to Basner et al. (2014), nonauditory effects of noise exposure were first recognized in occupational settings such as weaving mills. Now research has broadened from occupational noise exposure to recreational noise exposure as well. The discussion to follow will focus on occupational noise exposure only.

### **Occupational Safety and Health Administration**

The Occupational Safety and Health Act of 1970 was passed in the United States to prevent workers from being injured or killed on the job and required employees to provide safe work environments. As a result of this act, OSHA was formed. OSHA is responsible for providing training and assistance to workers and employees (OSHA, 2014). The specific workers' rights under the OSHA Act include the right to ask OSHA to inspect their work environment, use their rights under the law without the risk of

retaliation or discrimination, and receive appropriate training on hazards and OSHA standards for their workplace. The National Institute for Occupational Safety and Health is a division of the Centers for Disease Control and Prevention (CDC) and communicates recommended standards to regulatory agencies such as OSHA (CDC, 1998). Similarly, the Directive 2003/10/EC of the European Parliament and of the Council of 6 February 2003 on the minimum health and safety requirements regarding the exposure of workers to the risks arising from physical agents (e.g., noise) (Seventeenth individual Directive within the meaning of Article 16(1) of Directive 89/391/EEC), the European Agency for Safety and Health at Work lays down requirements for protection of workers from risks to their health including exposure to excessive noise that puts hearing at risk. These regulations are stricter than those set forth by OSHA in the United States (Goelzer et al., 2001). This work will focus on regulations for the United States as regulated by OSHA.

OSHA covers most workers in the United States including private sector workers, state and local government workers, and federal government workers. Those not covered by OSHA include individuals who are self-employed, immediate family members of farm workers that do not employ outside employees, and those who work in an environment where workplace hazards are regulated by another federal agency such as the Mine Safety and Health Administration or the Coast Guard (OSHA, 2014). Just a few of the standards required in most workplaces include providing fall prevention, prevention of infectious diseases, and preventing NIHL. OSHA regulations regarding noise exposure include five basic aspects: identification of exposure levels and monitoring of these levels, protection of workers from hazardous noise exposure,

annual hearing tests, annual worker training, and record keeping (Feuerstein & Chasin, 2009).

The OSHA standards specific to the prevention of NIHL can be found in the Occupational Safety and Health Standards, Subpart G: Occupational Health and Environmental Control (OSHA, *n.d.*). The criteria indicating the permissible duration and intensity of noise exposure is determined by measurements made on the A scale of a sound level meter. When noise levels are determined by octave band measurements the equivalent A weighted sound level may be determined with the use of Figure 1. This information is utilized to determine exposure limits for continuous noise exposure. According to OSHA (*n.d.*), noise is considered continuous when the variation in the noise level involves maxima at intervals of one second or less (OSHA, *n.d.*).

Permissible noise exposure limits are dependent upon the duration per day of exposure. It is generally accepted that exposure less than 75 dBA causes no measurable change in hearing regardless of the length of exposure (Feuerstein & Chasin, 2009). The permissible sound level dBA slow response is lower as the duration of exposure increases. For comparison purposes, 90 dBA is permissible for eight hours while 115 dBA is only permissible for  $\frac{1}{4}$  of an hour or less (OSHA, *n.d.*). Additionally, 105 dBA is permissible for one hour or less. When the daily exposure occurs in two or more periods of exposure, the combined effect should be considered.

When an employee's exposure time equals or exceeds an eight hour time weighted average of 85 dB the employer is required by OSHA standards to develop and implement a monitoring program (OSHA, *n.d.*). The monitoring program shall provide a

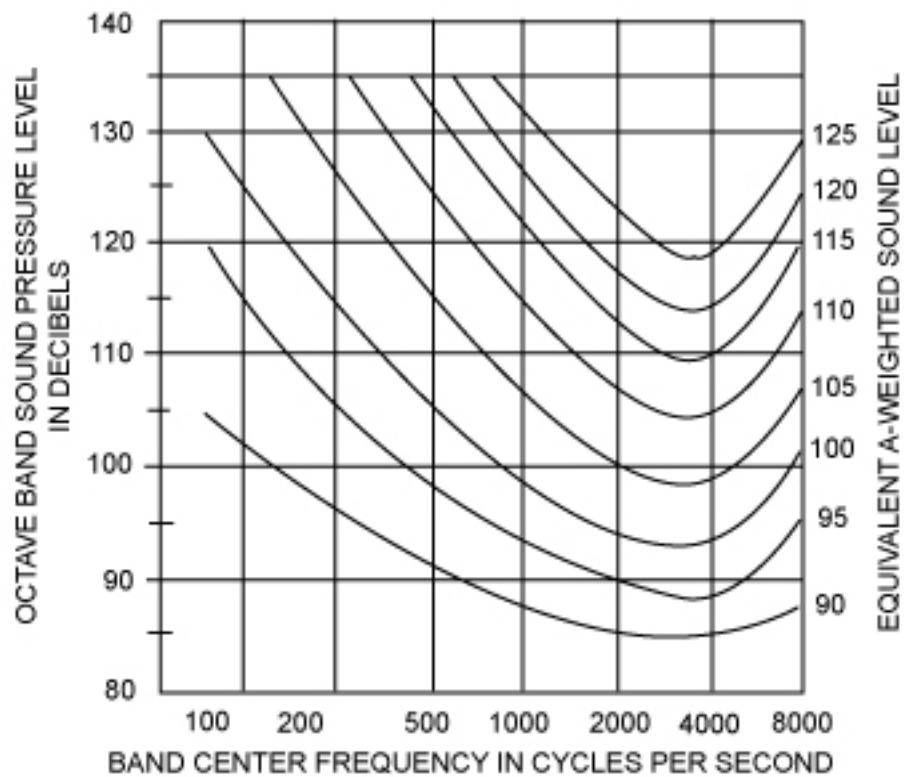


Figure 1. Equivalent sound level contours. Adapted from Occupational Safety and Health Administration: Occupational Safety and Health Standards Subpart G. Retrieved from [https://www.osha.gov/pls/oshaweb/owadisp.show\\_document?p\\_table=STANDARDS&p\\_id=9735](https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=9735).



strategy for appropriately identifying and including an employee in the hearing conservation program. Noise measurement equipment must remain calibrated and measurements must be performed any time there is a change in production, process, or equipment as well as when additional employees may be exposed to the previously mentioned action level.

## **Hearing Conservation**

The ACOEM's most recent guidance statement was published in 2012 and explains the crucial relationship between employers and the occupational and environmental physicians (Kirchner et al., 2012). This statement illustrates the importance of "a hierarchy of controls which prioritize the use of engineering controls over administrative controls and personal protective equipment" (Kirchner et al., 2012, p. 106). If the proper controls are in place, NIHL is preventable. The only clinically successful preventative measure against NIHL is a hearing protective device and the only treatment available is a hearing aid (Ohlemiller, 2008).

Hearing conservation is maintained with the use of the previously mentioned monitoring program. It is the responsibility of the employer to administer a continuous and effective hearing conservation program (OSHA, *n.d.*). Firstly, the hearing conservation program should be designed to appropriately identify employees for inclusion and enable the proper selection of hearing protectors. This provides both the company and the employee with information explaining the possible extent of noise hazard (Feuerstein & Chasin, 2009). The type of noise source and interference with communication should be factors considered as posing potential risks. Another factor is the worker complaints regarding noise levels including reports of temporary hearing loss

or tinnitus. Sound levels must be appropriately measured in any work environment with suspicion of risk for noise hazard.

Initially the OSHA regulations for protecting employees from NIHL were threefold: engineered reduction of the noise, limiting exposure time, and use of personal hearing protection. This was revised in 1983 to the “performance approach” (Feuerstein & Chasin, 2009, p. 689). With this change the engineered reduction of noise criteria was dropped and employers were allowed to develop their own approach to meeting the criteria. The use of personal hearing protection is the most widely used method of preventing NIHL and requires that employers provide appropriate hearing protection devices at no charge to the employee, that those devices fit properly, and that each worker must be trained in proper use and care of his hearing protection device.

The most efficient way to measure effectiveness of the hearing conservation program is to periodically monitor hearing thresholds. These routine hearing tests should be performed on any worker exposed to at or above the action level (Feuerstein & Chasin, 2009; OSHA, *n.d.*). The OSHA guidelines do require that a professional administer the testing including a baseline test, annual retests, worker training, and follow-up procedures. The puretone threshold procedure must include responses at 500, 1000, 2000, 3000, 4000, and 6000 Hz for each ear with at least 14 noise free hours preceding the test time (OSHA, *n.d.*). The baseline audiogram is to be obtained within the initial six months of employment and the retest must occur at least annually (Feuerstein & Chasin, 2009). A standard threshold shift has occurred if the average of 2000, 3000, and 4000 Hz is 10 dB worse than the average of the baseline audiogram keeping in mind that there is a frequency specific age adjustment to account for

presbycusis. The age correction is first applied to the annual audiogram. Then the three-frequency average for each ear is taken and compared to the baseline audiogram.

The hearing conservation program becomes quite complex once a significant threshold shift of 10 dB has been identified. The requirements for action to be taken include that the significant shift be present and that the average hearing loss of the same frequencies for that ear exceed 25 dB HL. OSHA is aware that some temporary shifts in hearing are due to medical conditions and requires that a confirmation retest take place within 30 days of the employer being made aware of the shift (Feuerstein & Chasin, 2009). Contrarily, if the shift is 25 dB or greater the retest must occur within 30 days of the date of the annual audiogram. If the shift is confirmed with the retest, the employer must notify the employee in writing. All threshold shifts are presumed to be due to noise exposure unless a physician or other licensed health professional determines that the shift is unrelated to occupational noise exposure. Once the shift is confirmed the professional in charge of the hearing conservation program can revise the baseline test to reflect the new thresholds. This is to avoid over-referrals for additional attention (Feuerstein & Chasin, 2009). The baseline may also be revised if the employee shows a significant improvement in hearing due to medical problems present at the baseline test that have since resolved. Without updating the baseline to reflect these better thresholds any future NIHL could go unnoticed.

Annual training is required for any worker with noise exposure at or above the action level (OSHA, *n.d.*). The worker training program must encompass information on the effects noise exposure, a discussion on various forms of hearing protection including advantages and disadvantages of each, and instruction on proper use and

care on each worker's hearing protection device. It is important for the employees to understand the reasoning for annual hearing retests and the consequences of improper or irregular use of hearing protection.

According to OSHA standards, employers must keep records of noise exposure measurements for a minimum of two years. Audiometric data must be kept for the duration of the affected worker's employment with the company and must be provided to the worker if they request this information. If under any circumstances the business is sold, these records must be transferred to the new owners and maintained in accordance with OSHA regulations.

### **Summary and Research Questions**

As presented throughout this review, NIHL is an epidemic affecting 10 million workers with another 30 million being at risk for NIHL (Dobie, 2008). According to Dobie (2008), the American Academy of Otolaryngology-Head and Neck Surgery has suggested that NIHL is more common than age related hearing loss. Often times NIHL goes unnoticed due to both the temporary nature of the initial effects or the delayed clinical changes as a result of anatomical and physiological auditory changes. PTSs are often not observed for decades following the exposure. Even in highly controlled studies the relationship between the amount of noise exposure and the resulting anatomic and physiological damage is variable (Stamper & Johnson, 2014).

Clinical protocols have primarily relied on behavioral measures of auditory function to evaluate changes resulting from exposure to intense noise. It is well known that PTSs are a result of permanent damage to cochlear structures including destruction of cochlear hair cells or damage to their mechano-sensory hair cell bundles (Kujawa &

Liberman, 2009). According to Kujawa and Liberman (2009), human research on noise exposure follows a paradigm that results in no hair cell death; however, there is observed swelling of cochlear nerve terminals resulting in a TTS. TTSs have been utilized as a safe test of susceptibility to PTS (Yates et al., 1983). The noise contributing to a TTS has no morphological effect on the cochlea but can be attributed to metabolic changes with the outer hair cells of the cochlea, which are essential to hearing sensitivity and frequency selectivity and can be observed in the electrical response of the outer hair cells in the cochlea or by measuring changes to OAE responses (Patuzzi, 1998; Quaranta et al., 2003). Recent studies in mice (Kujawa & Liberman, 2009) and guinea pigs (Lin et al., 2011; Furman, Kujawa, & Liberman, 2013) have challenged the belief that temporary NIHL does not result in permanent auditory damage while also suggesting that current clinical protocols for evaluating NIHL may be insensitive to early detection of auditory damage.

OAEs have been proposed to provide valuable information in the early detection of NIHL. Specifically, DPOAEs are considered the most sensitive evoked-response test for detecting OHC damage in both ototoxicity and NIHL (Kim et al., 2005). This is largely due to the fact that OAEs reflect some of the mechanical properties in the cochlea and are noninvasive and objective (Engdahl & Kemp, 1996). OAEs are a preneural phenomenon, an indirect measure of OHC function, and are vulnerable to acoustic trauma, hypoxia, and ototoxic medications. OHCs are more susceptible to damage than IHCs, which is most likely due to structural reasons. As described previously, OHCs are coupled to the motion of the BM, are connected to the tectorial membrane through the tallest stereocilia, and are not surrounded by supporting cells

leading to more exposure to BM motion (Slepecky, 1986). OAEs are relatively easy to record, quick to obtain in the clinical setting, and useful for corroborating audiometric data. Engdahl & Kemp (1996) found that the use of these low level DPOAEs is a safe and sensitive monitor of susceptibility to noise.

Lapsley-Miller et al. (2006) suggest that it is possible the OAEs indicate noise-induced changes in the inner ear that are undetected in audiometric testing and, as a result, may be a diagnostic predictor for NIHL risk. Similarly, Montoya et al. (2008) suggest that the cochlear impairment as a result of MP3 player noise may be detectable in OAE measurements prior to changes in other clinical tools. Vlcnck et al. (1999) also suggest that OAEs are more sensitive than the behavioral audiogram in detecting subtle changes in OHC function. TEOAE and DPOAE responses in this study were significantly reduced and did not fully recover in the 4000 Hz frequency range even though the pure tone audiogram did not show hearing loss.

DPOAE I/O functions in most species consist of two components, one elicited at low stimulus levels and the other elicited at high stimulus levels. It is well known that the low stimulus level of the DPOAE I/O function is reduced or eliminated when the hair cells are damaged while the latter remains relatively resistant to cochlear damage (Engdahl & Kemp, 1996). DPOAE I/O functions have been found to be compressive in normal hearing subjects and exhibit strong saturation at moderate primary tone levels. In the hearing impaired ears, however, the reductions of DP level are greatest at lowest stimulus levels and smallest at highest stimulus levels resulting in a linearized DP I/O function. Kummer et al. (1998) suggest that due to these findings DPs should be

measured at lower primary tone levels in addition to higher levels to aid in the prediction of the hearing threshold.

Nam and Won (2004) suggested that the ECoChG is a useful tool for the early detection and monitoring of NIHL. This study found that the SP/AP amplitude ratio was a very sensitive measure of noise-induced change. This was based on the fact that the four frequency pure tone average thresholds did increase in the TTS phase but did not exceed the normal limit. The SP/AP amplitude ratio of the ECoChG, however, did exceed the normal limit. Nam and Won (2004) believe that the SP/AP amplitude ratio is a more sensitive measure of noise-induced cochlear change than TTSs and that an elevated SP/AP amplitude ratio indicates temporary, reversible damage. They also suggest that these results support the notion that ECoChG may be able to detect subtler changes in functional integrity than just cochlear hydrops.

Kim et al. (2005) suggest that ECoChG should show greater sensitivity than DPOAEs in detecting small, subtle functional changes making it more useful in predicting noise-induced TTSs. This study determined that ECoChG is more sensitive and specific for detecting a noise-induced TTS than DPOAEs when between the TTS phase and the stage earlier than mild hearing loss. DPOAEs, on the other hand, are more suitable between the mild and permanent hearing loss of 25 dB to 40 dB. The general application of ECoChG in inner ear diseases has been prevented due its high sensitivity to subtle changes of anatomical and physiological structures.

The intertest and intratest reliability of ECoChG is good, especially when evoked by click stimulation, allowing for the detection of a real change in cochlear electrophysiology; however, there is no standard clinical protocol at this time (Nam &

Won, 2004). There are currently two general recording approaches: TT and extratympanic (ET). Both approaches have advantages and disadvantages. The TT approach produces large components of the response with minimal signal averaging due to its close proximity of the recording electrode to the response generators (Ferraro, 2010). The ET approach requires more signal averaging and results in a smaller magnitude of response. The advantage of the ET approach, however, is that a physician is not required to place the electrode. Most clinics are currently using an ET approach (Ferraro, 2010). A gold foil electrode wrapped around a foam insert (TIPtrode™) can serve as one option for an ET approach, with the TIPtrode™ being placed in the ear canal. This is most comfortable for the patient but results in a significantly smaller magnitude of the response. A compromise in increased magnitude and decreased signal averaging without significant patient discomfort is the use of the Lilly TM-Wick. The Lilly TM-Wick is a single use, disposable electrode for obtaining ECoChG recordings (IHS, 2015). One end of the Lilly TM-Wick is a soft cotton tip (wick) that has been soaked in a low impedance electrode gel and then dehydrated for extended shelf life. The wick is located on the end of a thin electrode cable that is connected to an electrode lead connector. This electrode rests against the TM and is still relatively comfortable for the patient. Due to the closer proximity to the generator, the response magnitude is significantly increased when compared to TIPtrode™ responses. At this time there has been only one study evaluating the reliability of these electrode placements for ECoChG (Roland et al., 1993). Additionally, the test-retest reliability of differing stimulus rates has not been evaluated. A faster rate will result in some adaptation of the AP response while the SP is theorized to be relatively



unaffected (Ferraro, 2010). Experiment 1 was designed to address the following research question: What is the effect of test, electrode, and rate on SP amplitude, AP latency, AP amplitude, SP/AP amplitude ratio, and SP/AP area ratio? It was hypothesized that there will be no effect of test. There would, however, be an effect of electrode type and rate. That is, Lilly TM-Wick responses were hypothesized to have a significantly larger amplitude than those obtained with a TIPtrode<sup>TM</sup>. It was also hypothesized that the faster rate of 77.7/s would result in longer latencies, smaller amplitudes, and larger SP/AP amplitude and area ratios. There was no anticipation of any interactions of variable effects.

In Experiment 2, an examination of the effect of a controlled noise exposure on behavior threshold responses was undertaken. The noise stimulus utilized in Experiment 2 is known to provoke a TTS in humans of approximately 10-15 dB around 3000 Hz after exposure (Engdahl & Kemp, 1996; Hooks-Horton et al., 2001). Specifically, auditory thresholds differences were examined as a function of frequency, ear, and gender. It was hypothesized that there would be a main effect of frequency and a frequency by test interaction with greater changes at certain frequencies (i.e., 3000 Hz). There was no anticipation of a gender effect nor any additional interactions. The association between auditory threshold differences and acoustic reflex indices were also examined. It was hypothesized that those with highest intensity acoustic reflex thresholds should exhibit the most change in auditory thresholds. Additionally, it was hypothesized that those with the greatest change in auditory threshold should exhibit the longest acoustic reflex latencies.

To date, there is limited research examining the effects of noise on DPOAEs (Engdahl and Kemp, 1996; Kummer et al., 1998; Marshal & Heller, 1998; Vinck et al., 1999; Lapsley-Miller et al., 2006; Wooles et al., 2015) and ECoChG (Nam and Won, 2004; Kim et al., 2005). OAEs provide objective information on the integrity of outer hair cell function and have been suggested to be particularly useful for assessing damage due to noise overexposure (Marshal & Heller, 1998). As a result of the high sensitivity of low levels to noise exposure, the use of these low level DPOAEs is a safe and sensitive monitor of susceptibility to noise (Engdahl & Kemp, 1996). Vinck et al. (1999) found that OAEs are more sensitive than the behavioral audiogram in detecting subtle changes in OHC function. Similarly, Lapsley-Miller et al. (2006) found that the average amplitudes of OAEs decreased significantly while there were no statistically significant changes in audiometric thresholds. Conversely, Wooles et al. (2015) found that DPOAE amplitudes and pure tone audiometric thresholds exhibit poor correlation, which does not support DPOAE use to predict hearing thresholds clinically. With regards to ECoChG, Nam and Won (2004) found that the SP/AP amplitude ratio is a more sensitive measure of noise-induced cochlear change than TTs and that an elevated SP/AP amplitude ratio indicates temporary, reversible damage. It has also been noted that the shape of the electrocochleogram changes gradually with TTs in that the AP becomes more obtuse and wider and the location of the SP falls. Kim et al. (2005) concluded that DPOAEs are not the most sensitive test for detecting OHC damage. It is apparent that research in this area is equivocal. In addition, this is the first study also examining gender effects.

In Experiment 3, an examination of the effect of a controlled noise exposure on DPOAE I/O function responses was undertaken. Specifically, DPOAE absolute amplitude differences were examined as a function of gender, ear, level, and frequency. It was hypothesized that DPOAE absolute amplitudes would be decreased following noise exposure. No effects of gender or frequency were anticipated for DPOAE I/O function thresholds; however, an interaction is expected with greater changes at certain frequencies (Kummer et al., 1998). It was conjectured that greater changes will be observed around 3000 Hz (Engdahl & Kemp, 1996).

Finally, in Experiment 4, an examination of the effect of controlled noise exposure on ECoChG responses was undertaken. Specifically, ECoChG indices differences were examined as a function of gender and ear. ECoChG results were hypothesized to decrease in AP amplitude, increase in SP amplitude, AP latency, and SP/AP amplitude ratio, and exhibit no change in SP/AP area ratio (Kim et al., 2005; Nam & Won, 2004). No effects of gender or ear were anticipated and no interactions were anticipated.

## CHAPTER II: EXPERIMENT 1 – COMPARING TWO ELECTRODES IN TERMS OF RELIABILITY AND RATE

ECochG is a method of recording stimulus-induced potentials of the cochlea and auditory nerve and is considered an objective parameter used in the diagnosis of Ménière's disease. A histological marker for Ménière's disease is the presence of hydrops in the endolymphatic space (Moon et al., 2012). In 67 patients with Ménière's disease symptoms including fluctuating hearing loss, episodic vertigo, and tinnitus, Gibson, Moffat, and Ramsden (1977) found that the SP response was enhanced relative to the AP component. These results were believed to be directly related to the presence of endolymphatic hydrops. It has been suggested that "the basilar membrane is deflected toward the scala tympani in cases of endolymphatic hydrops, and this bias acts on sensory cells" (Moon et al., 2012, p. 204-205). The ultimate result is the generation of a larger than normal DC component and, consequently, a larger SP. Additionally, previous research also demonstrates that the use of a fast stimulus rate fatigues the AP allowing for better visualization of the SP (Coats, 1981; Densert et al., 1994; Gibson et al., 1977; Marangos, 1996; Wilson & Bowker, 2002; Wuyts et al., 2001).

Even though ECochG is currently the most studied and well-known clinical method of detecting increases in pressure in the endolymphatic system of the inner ear, there remain many recording challenges including the lack of reliable normative data and recording standards (Hall, 2007). The primary technical consideration while recording is noise. ECochG requires a small electrode placed as close to the response generator as possible for the best signal-to-noise ratio. The TM has been suggested as

the optimal noninvasive recording site for adults (Ferraro, 2010). Research has also suggested that ECoChG recordings measured from the lateral surface of the TM result in reliable tests that can be used for assessment and reassessment of normal-hearing subjects' SP/AP amplitude ratios (Park & Ferraro, 1999). To date, several studies have reported test-retest variability of ECoChG indices with TT (Bergholtz, Hooper, & Mehta, 1976; Densert et al., 1994) and ET (Mori, Matsunaga, & Asai, 1981; Roland et al., 1993) recordings, however, there have been no investigations of test-retest reliability of different ET electrode types at differing stimulus rates on indices of ECoChG including the SP/AP area ratio. Specifically, what is the effect of test, electrode, and rate on SP amplitude, AP latency, AP amplitude, SP/AP amplitude ratio, and SP/AP area ratio?

## **Methods**

### **Participants**

Participants were 18 English speaking Caucasians with a negative history of loud noise exposure within 48 hours prior to data collection. They had no significant history of neurological, otological, and/or communication disorders by self-report. Participants ranged in age from 20 to 30 years ( $M = 25.2$ ,  $SD = 2.9$ ; 14 females and 4 males). One ear was tested on each participant. Right and left ears were counterbalanced for a total of 18 ears. All participants had normal hearing sensitivity defined as pure tone thresholds at octave frequencies from 250 Hz to 8000 Hz  $\leq 15$  dB HL (American National Standards Institute, 2010). Participants also had normal middle ear function defined as  $Y_{tm} = 0.3$ -1.50 mmho,  $TW = 35.80$ - 95.00 daPa,  $V_{ea} = 0.9$ -1.80 cm<sup>3</sup>, and  $TPP \pm 50$  daPa (Roup et al., 1998; Marshall, Heller, & Westhusin, 1997). Mean hearing thresholds for all participants as a function of frequency and ear are displayed in Table

1. Mean tympanometric indices for all participants as a function of ear are displayed in Table 2.

## **Apparatus**

A Grason-Stadler (GSI) 61™ audiometer was utilized to obtain behavioral thresholds. Tympanometric measures were obtained using a GSI TympStar™. ECoChG data acquisition was performed using the Intelligent Hearing Systems (IHS) Smart EP evoked potential system. Both Lilly TM-Wick and gold-foiled TIPtrode™ electrodes were utilized to record responses and muscle artifact for signal averaging techniques. All stimuli were presented via ER-3A insert earphones.

## **Experimental Signal**

ECoChG responses were obtained to 100  $\mu$ s click stimuli of alternating polarity. The clicks were presented at 90 dB nHL with a slow rate (7.7 pulses per second) and a fast rate (77.7 pulses per second) and 1,024 sweeps were averaged. The amplitude as a function of time waveforms for electric and acoustic click stimuli of condensation and rarefaction polarity are presented in Figures 2 through 5.

Waveforms were initially generated using SpectraPRO-FFT Spectral Analysis System software (version V.3.32.17) on a Dell Latitude D630 laptop computer. For analyses of acoustic stimuli, the signals were generated by the IHS Smart EP system. The signal was routed in series from the insert earphone to a 2cc coupler (Brüel and Kjær type DB 0138), pressure condenser microphone (Brüel and Kjær type 4144), and sound level meter (Brüel and Kjær Type 2231). The signal was then routed to a Dynamic Signal Acquisition System (model ST191DSA) signal generator that interfaced with the Dell Latitude laptop containing the SpectraPRO software. For analyses of

Table 1. *Mean Hearing Thresholds (dB HL) and Standard Deviations as a Function of Frequency and Ear (N = 18).*

		Frequency (Hz)							
		250	500	1000	2000	3000	4000	6000	8000
Ear									
Right		8.3	8.1	6.4	6.7	5.0	3.3	0.6	0.0
(n = 9)		(4.2)	(4.2)	(3.8)	(4.5)	(4.9)	(5.9)	(4.5)	(8.2)
Left		9.4	8.9	7.2	6.7	4.4	3.6	1.7	-0.6
(n = 9)		(4.8)	(5.8)	(4.3)	(6.6)	(5.9)	(5.4)	(5.7)	(7.8)

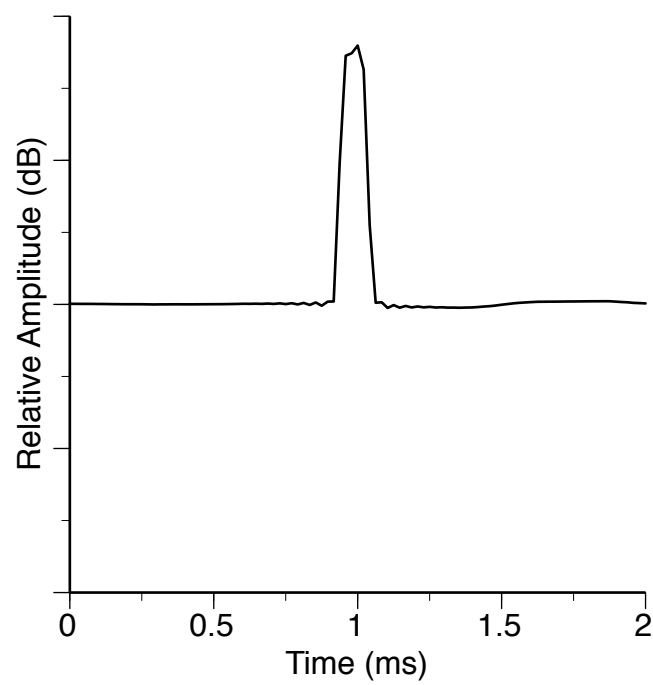
*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

Table 2. *Mean Tympanometric Indices and Standard Deviations as a Function of Ear (N = 18).*

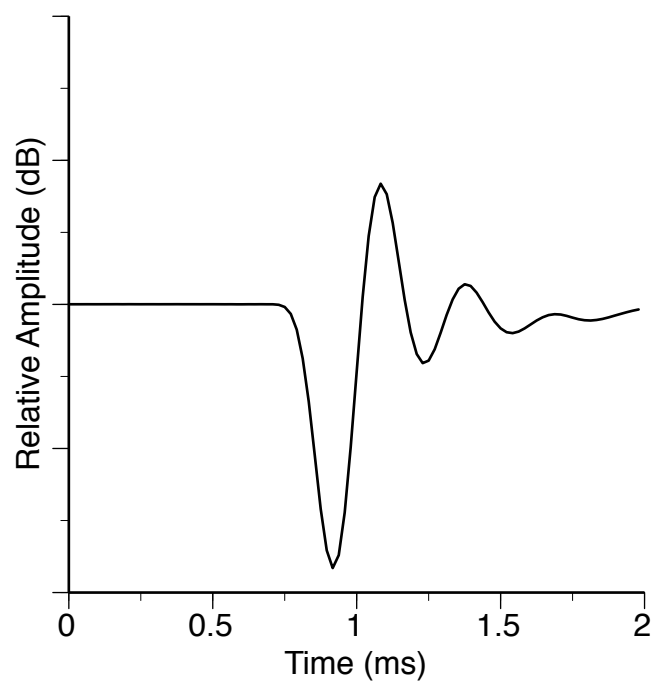
		Y <sub>tm</sub>	TW	TPP	V <sub>ea</sub>
Ear					
	Right	0.9	84	20	1.4
	(n = 9)	(0.6)	(34)	(11)	(0.3)
	Left	0.9	85	19	1.4
	(n = 9)	(0.6)	(43)	(9)	(0.3)

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

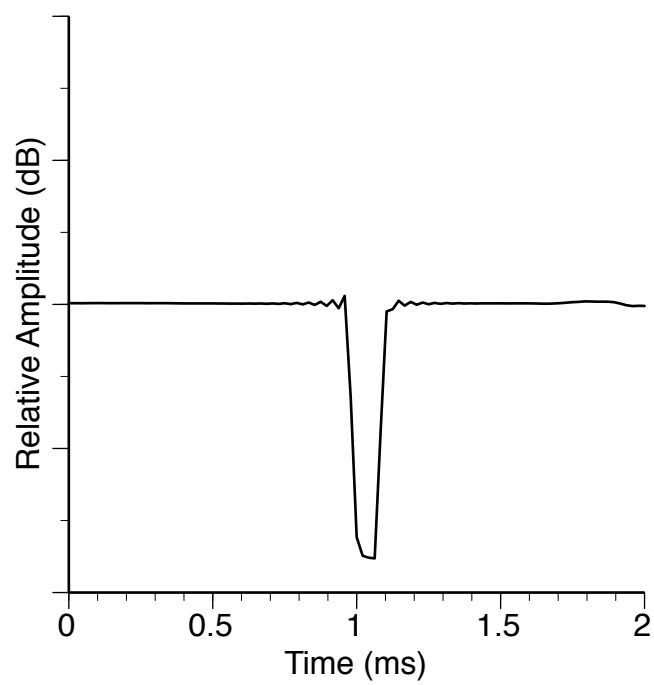




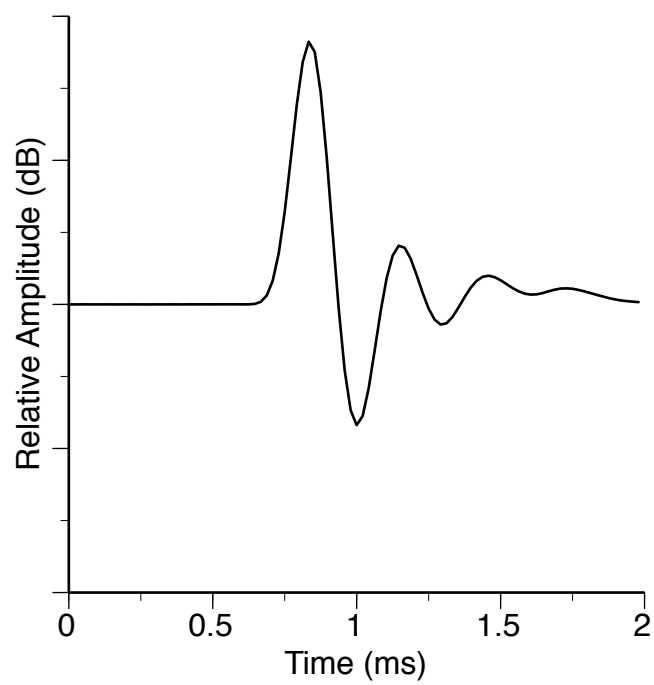
*Figure 2.* Amplitude as a function of time for a condensation polarity electric click.



*Figure 3.* Amplitude as a function of time for a condensation polarity acoustic click.



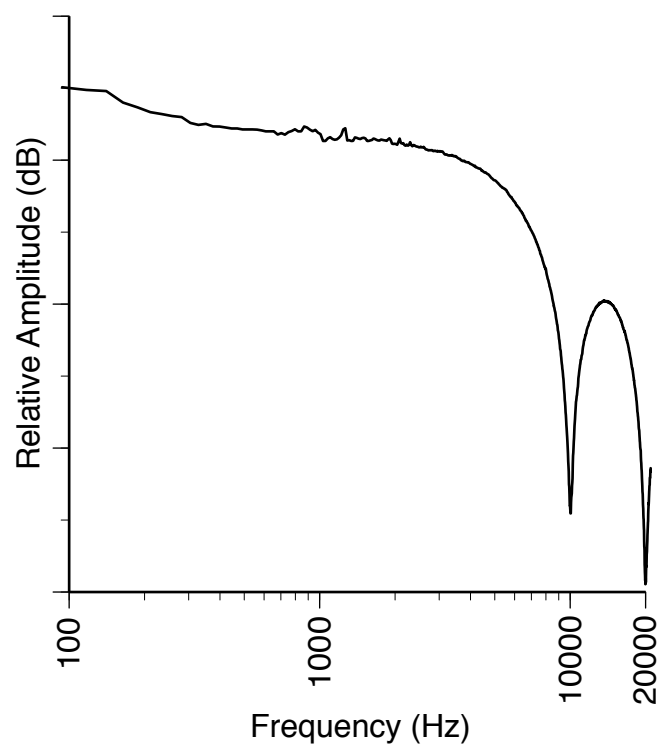
*Figure 4.* Amplitude as a function of time for a rarefaction polarity electric click.



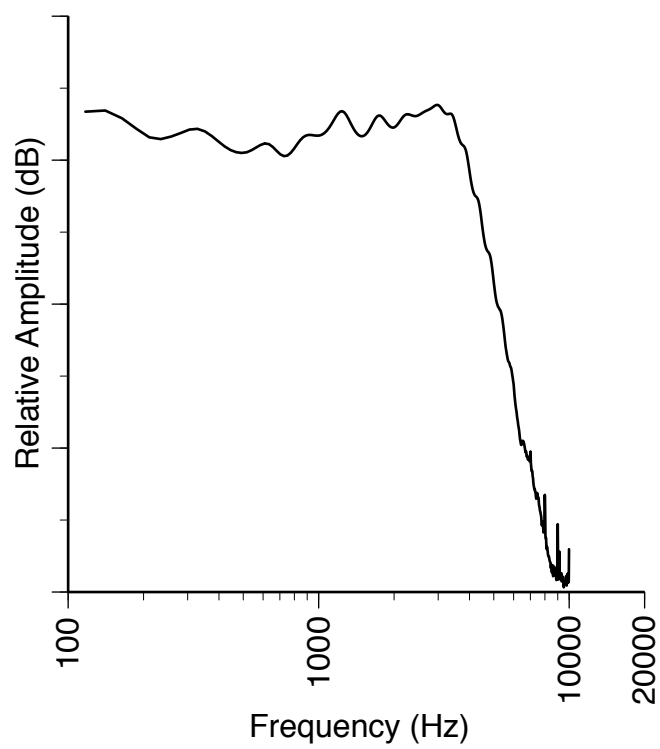
*Figure 5.* Amplitude as a function of time for a rarefaction polarity acoustic click.

electrical stimuli, the signal was also generated by the IHS Smart EP system and was transmitted directly from the IHS Smart EP system to the Dynamic Signal Acquisition System (model ST191DSA) signal generator that interfaced with the Dell Latitude laptop containing the SpectraPRO software. Data points were copied as text files and saved using Microsoft Notepad. These points were then imported into Excel files, saved, and exported into Delta Graph. Delta Graph was used to generate graphs. SpectraPRO-FFT Signal Analysis System software was also used to perform Fast Fourier Transforms (FFTs) on the alternating polarity electric and acoustic click (see Figures 6 and 7).

To configure the FFTs four settings were utilized; the smoothing window, the sampling rate, the decimation ratio, and the FFT size. The smoothing window prevents any smearing of the spectrum from a single line to adjacent lines. To overcome any leakage of the signal the signal level is forced to zero at the beginning and ending of the time series. The sampling rate represents how many times per second the analog signal was sampled to construct the digital representation of the signal. The decimation ratio is the ratio at which the file is reproduced with a lower sampling rate. If, for example, the decimation ratio was set to 4:1, the SpectraPRO software would average four samples together to produce one sample. A decimation ratio of 1:1, on the other hand, does not down sample the original signal. Finally, the FFT size is related to the frequency resolution of the file as well as the number of spectral lines. The number of spectral lines, or points, is exactly one-half of the FFT size. Consequently, the larger the FFT size, the higher the frequency resolution of the FFT. The FFTs for the click stimuli were generated using a Hanning window, a sample rate of 48,000 Hz, a



*Figure 6.* FFT of an alternating polarity electric click.



*Figure 7.* FFT of an alternating polarity acoustic click.

decimation ratio of 1:1, and a FFT size of 2,048.

## **Procedure**

The East Carolina University and Medical Center Institutional Review Board approved this research study prior to data collection or participant recruitment (see Appendix A). Participants were recruited from the East Carolina University student body to include the School of Allied Health Sciences as well as the Department of Communication Sciences and Disorders. Participants were recruited on a volunteer basis and an informed consent was reviewed and signed by each participant prior to data collection (see Appendix B). All participants were required to meet the previously discussed inclusion criteria.

Behavioral thresholds and tympanometric measures were obtained for both ears while participants were seated in a double walled sound treated audiometric suite (Industrial Acoustics Corporation) meeting the specifications for permissible ambient noise (American National Standards Institute, 1999).

ECochGs were obtained for the initial test and repeat test for both Lilly TM-Wick electrodes and TIPTrodes™ with at least one replication for each condition. Participants were comfortably seated in a recliner in a quiet exam room for all conditions. Each condition was counterbalanced according to a digram-balanced Latin squares design (Wagenaar, 1969). Prior to data collection Signa-Gel® Electrode Gel was applied to the Lilly TM-Wick electrodes. These were then soaked in a saline solution for ten minutes. Participants were instructed to sit quietly with little movement throughout the test. A horizontal recording montage was utilized with the noninverting electrode on the lateral surface of the TM for recording with Lilly TM-Wick electrodes or the lateral external



auditory canal for TIPtrode™ recordings, the inverting electrode on the contralateral mastoid, and the ground electrode on the high forehead ( $F_{pz}$ ). The skin was cleaned prior to electrode application by gently scrubbing NuPrep skin prep gel on the contralateral mastoid,  $F_{pz}$ , and the lateral portion of the external auditory canal. The TIPtrode™ electrodes were gently squeezed between the fingertips, placed into each participant's test ear so the outer portion was even with the canal, and held there until the foam tip had time to expand in the ear canal. Lilly TM-Wick placement was verified by having the participant report when they heard the electrode bump against the TM, at which time the electrode lead was carefully taped anteroinferior to the intertragal notch and held while an insert earphone was inserted in the same manner as the TIPtrode™. Interelectrode impedances were kept at or below 7,000  $\Omega$  when testing with Lilly TM-Wick electrodes and at or below 1,000  $\Omega$  for TIPtrode™ electrodes. The recorded electroencephalogram (EEG) was amplified 100,000 times and bandpass filtered (10 to 1,500 Hz). Each recording contained 1,024 samples that were averaged and replicated for rates of 7.7/s and 77.7/s.

### **Electrophysiological Waveform Analysis**

The SP waveform component was analyzed in terms of amplitude and the AP waveform component was analyzed in terms of amplitude and latency. The SP/AP amplitude ratio and SP/AP area ratio were also calculated and analyzed. The baseline of the response was identified at the onset of the initial negative deflection of the SP and the AP was the first negative going peak after one millisecond (Ferraro & Tibbils, 1999; Ferraro, 2010). The SP was defined as the highest point of the shoulder of the ascending portion of the response, or the leading edge of the AP (Moon et al., 2012).

Amplitudes were measured from the component trough to the baseline. The SP/AP area ratio was calculated in the IHS Smart EP system in accordance with recommendation from IHS by marking the amplitude of the base at the point in time following the AP trough where the response passed through the initial baseline amplitude.

## **Results**

### **Statistical Analyses**

All descriptive and inferential analyses were conducted with IBM SPSS Statistics for Mac (Version 23.0.0.0). Table 3 and Figure 8 show the percentage of ECoChG responses as a function of test, electrode, and rate. Measurable ECoChG responses were not obtained for all experimental conditions. Initially, logistic regression analyses were undertaken to examine predictor values of test, electrode, and rate for SP and AP response presence or absence. The analyses revealed that electrode, *Wald statistic* (1) = 10.85,  $p = .001$ , and rate, *Wald statistic* (1) = 14.18,  $p < .001$ , were statistically significant predictors of an SP response. It was also found that electrode, *Wald statistic* (1) = 11.35,  $p = .001$ , and rate, *Wald statistic* (1) = 13.61,  $p < .001$ , were statistically significant predictors of an AP response. That is, SP and AP responses were more apt to be present when recorded with a Lilly TM-Wick electrode and at a slow rate of 7.7/s. Representative waveforms for ECoChGs to click stimuli as a function of electrode type and stimulus rate are shown in Figure 9.

The test-retest reliability of ECoChG with two separate electrode types was examined in four ways. First, Pearson's product-moment correlation coefficients ( $r$ ) were determined to examine the association between initial test and retest of the five

Table 3. *Percentage of Responses (%) as a Function of Test, Electrode, and Rate for SP Amplitude and AP Amplitude.*

Electrode	Rate	Initial Test		Retest	
		SP Amplitude	AP Amplitude	SP Amplitude	AP Amplitude
Lilly-TM Wick					
	7.7/s	100%	100%	94%	100%
	<i>N</i>	18	18	17	18
	77.7/s	89%	89%	89%	89%
	<i>N</i>	16	16	16	16
TIPtrode™					
	7.7/s	94%	94%	94%	94%
	<i>N</i>	17	17	17	17
	77.7/s	44%	44%	44%	61%
	<i>N</i>	8	8	10	11

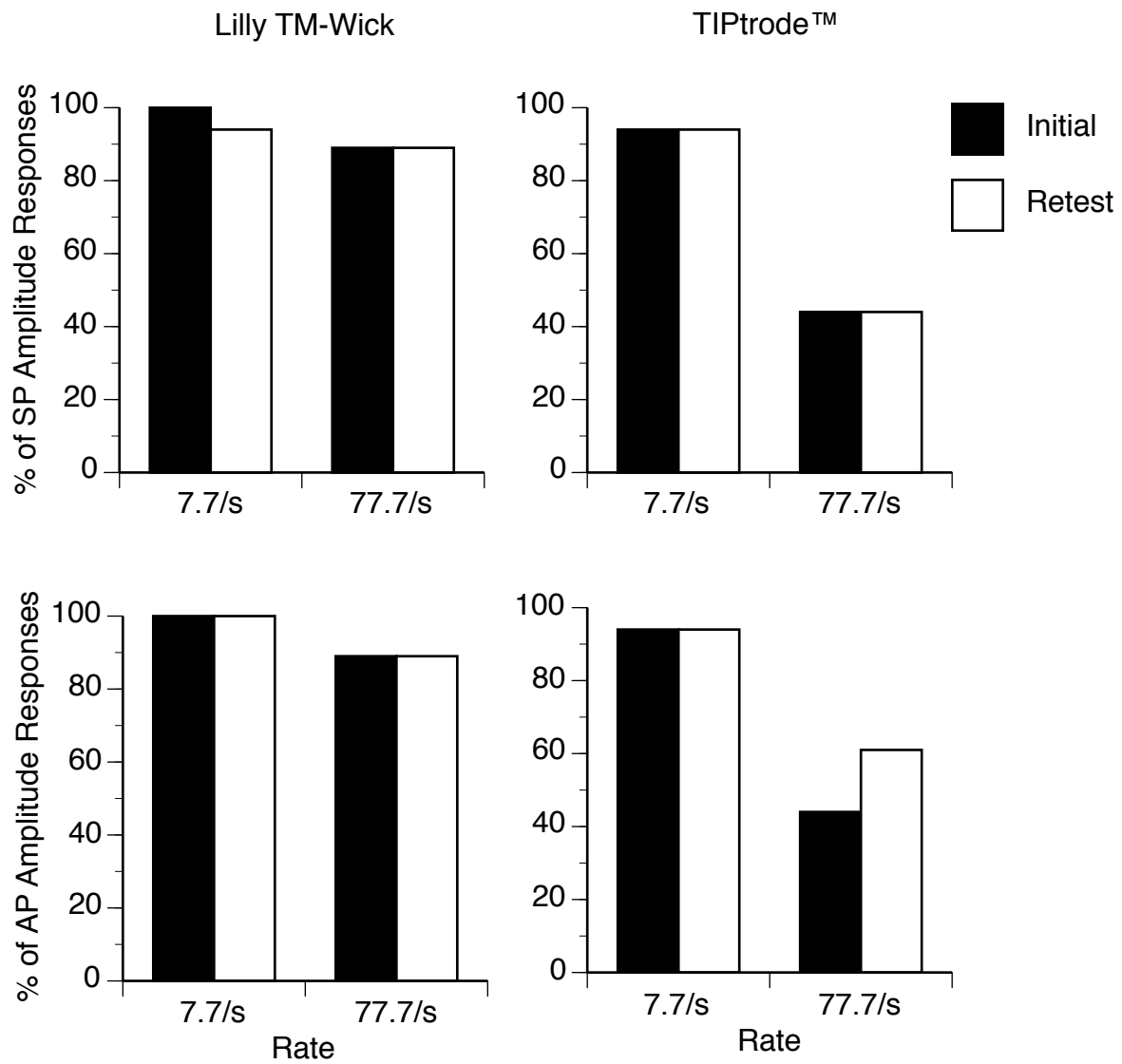
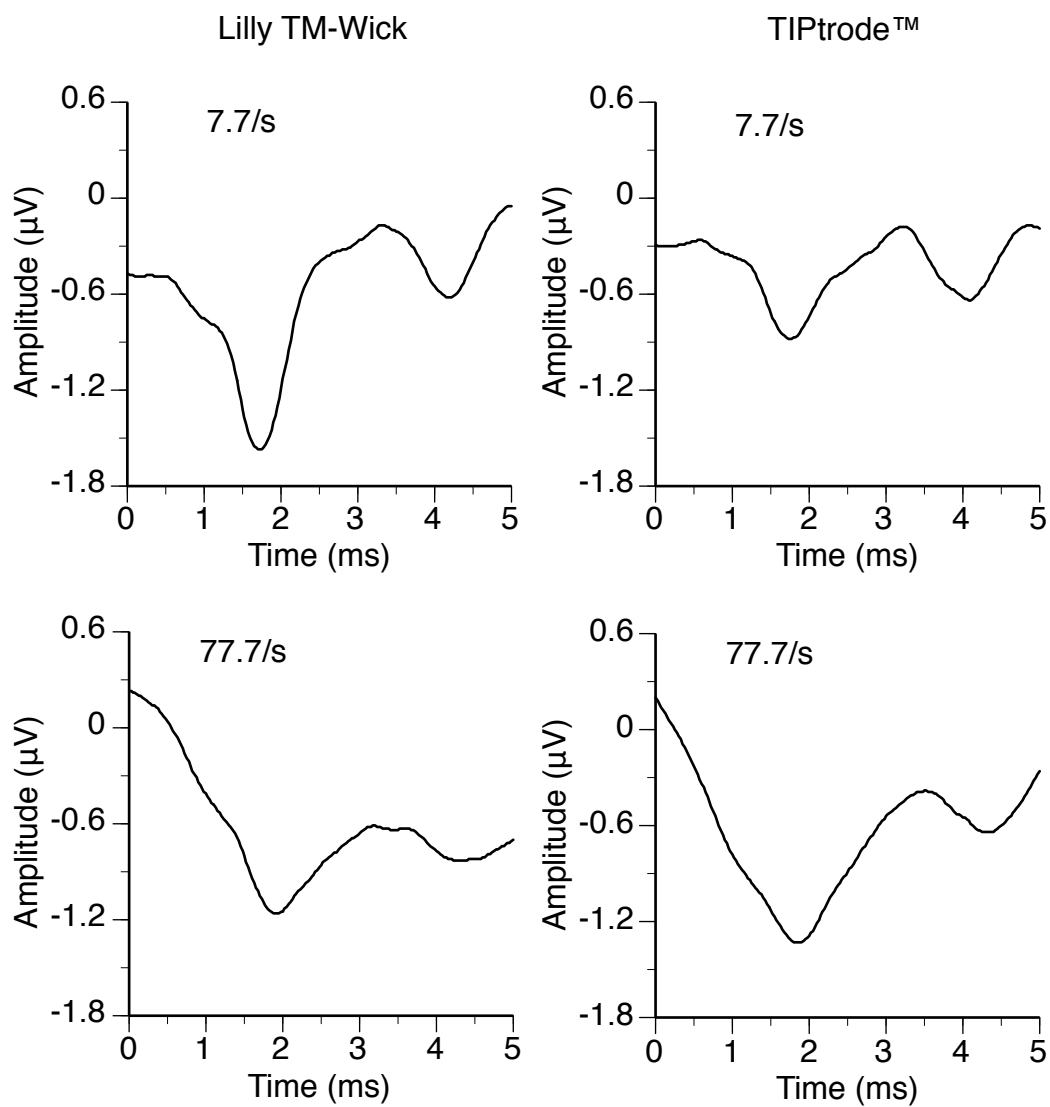


Figure 8. Percentage of presence of SP amplitude and AP amplitude responses as a function of test, electrode, and rate.



*Figure 9.* Representative ECoG waveforms from participant 5 as a function of electrode type and stimulus rate.

ECochG indices for both electrode types. There were statistically significant correlations between initial test and retest for the following ECochG indices when using a Lilly TM-Wick electrode: SP amplitude ( $r = .51, p = .001$ ), AP latency ( $r = .84, p < .001$ ), AP amplitude ( $r = .39, p = .02$ ), SP/AP amplitude ratio ( $r = .49, p < .01$ ), and SP/AP area ratio ( $r = .49, p < .01$ ). The bivariate scatterplots of these data are presented in Figures 10 to 14. For testing with TIProdes™, significant correlations between initial test and retest were found for AP latency ( $r = .53, p = .01$ ), AP amplitude ( $r = .61, p < .01$ ), SP/AP amplitude ratio ( $r = .52, p = .01$ ), and SP/AP area ratio ( $r = .50, p = .02$ ). The bivariate scatterplots of these data are also presented in Figures 10 to 14.

Second, five separate three-factor linear mixed model analyses of variance (ANOVA) with repeated measures were performed to determine the effect of test, electrode, and rate on SP amplitude, AP latency, AP amplitude, SP/AP amplitude ratio, and SP/AP area ratio. This ANOVA model can accommodate missing data in a repeated measures design. The repeated measures were modeled with an autoregressive (order 1) covariance metric. The choice of the covariance structure was based on goodness of fit statistics (i.e., -2 Res Log Likelihood, Akaike's information criterion, Hurvich and Tsai's Criterion, Bozdogan's Criterion, and Schwarz's Bayesian Criterion). Results for each dependent variable will be discussed below.

Third, due to limitations of the correlation and statistical significance to assess reliability, test-retest differences were also examined for each electrode with all five ECochG indices. The analyses included construction of boxplots and an examination of mean differences and their 95% confidence intervals.

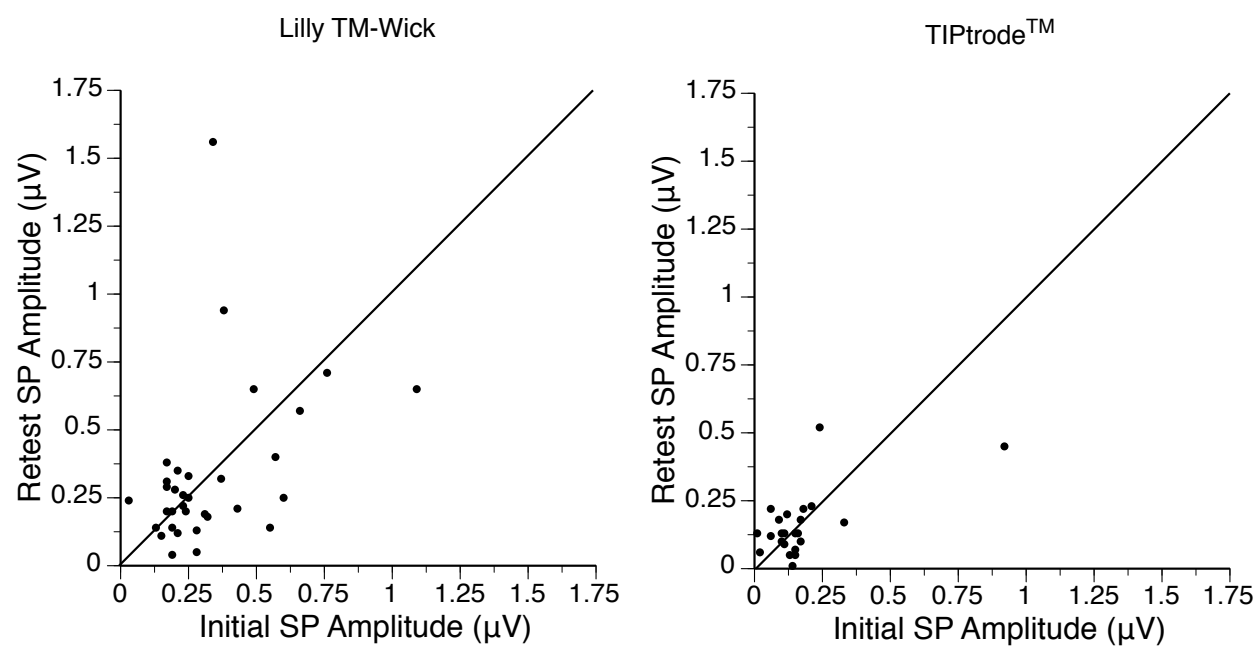
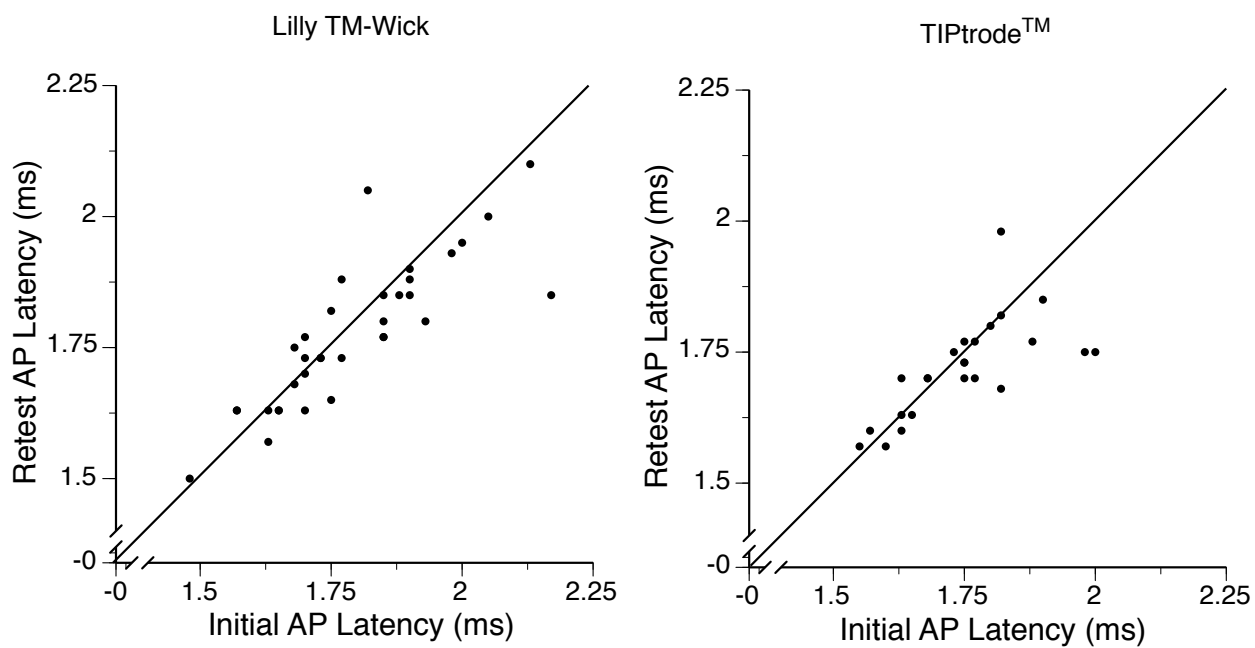
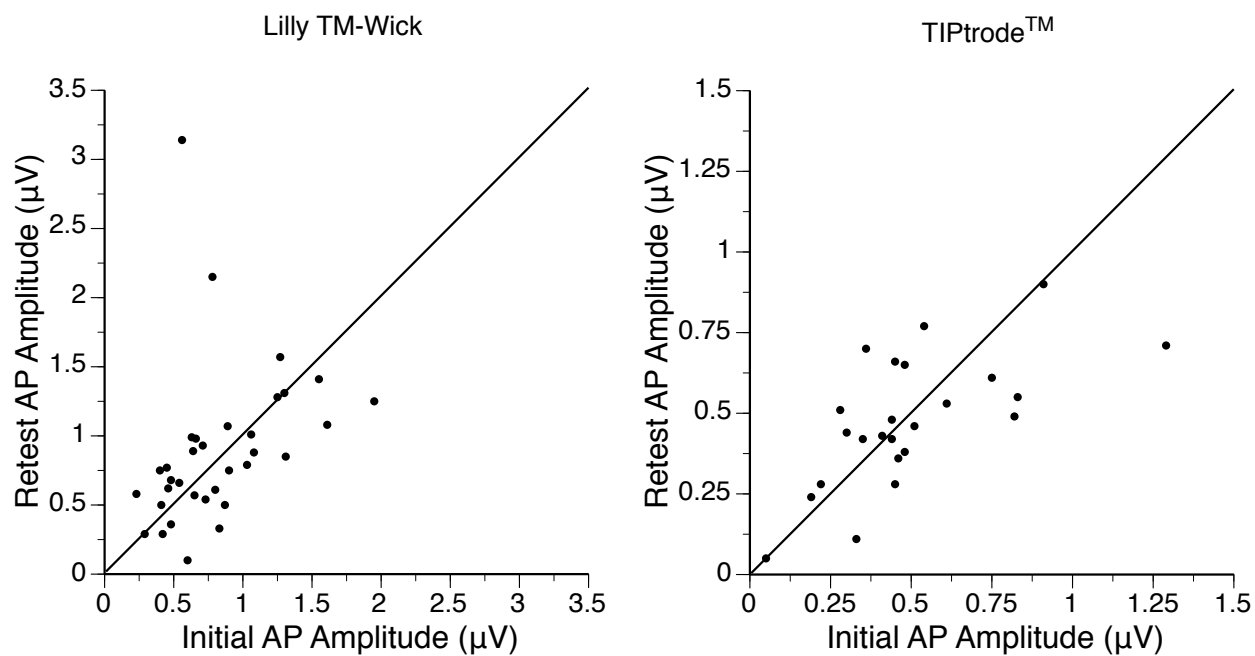


Figure 10. Bivariate scatter plots with line of equality of SP amplitude ( $\mu\text{V}$ ) for initial test and retest as a function of electrode.



*Figure 11.* Bivariate scatter plots with line of equality of AP latency (ms) for initial test and retest as a function of electrode.





*Figure 12.* Bivariate scatter plots with line of equality of AP amplitude ( $\mu\text{V}$ ) for initial test and retest as a function of electrode.

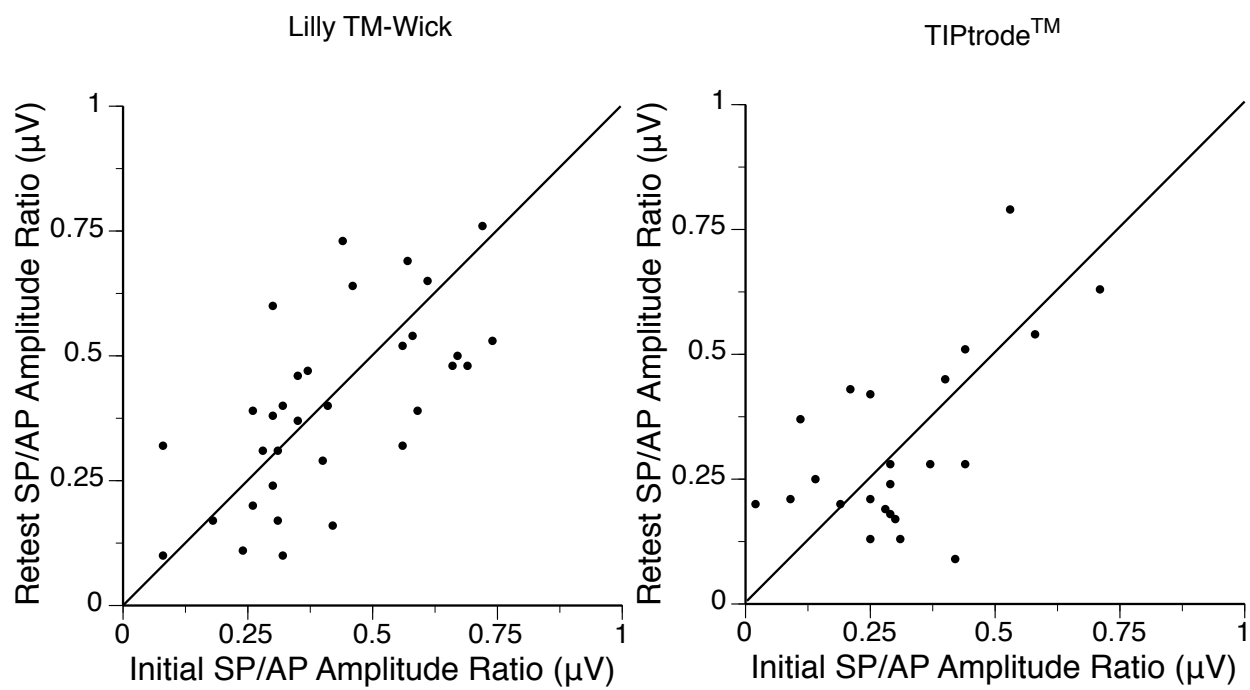
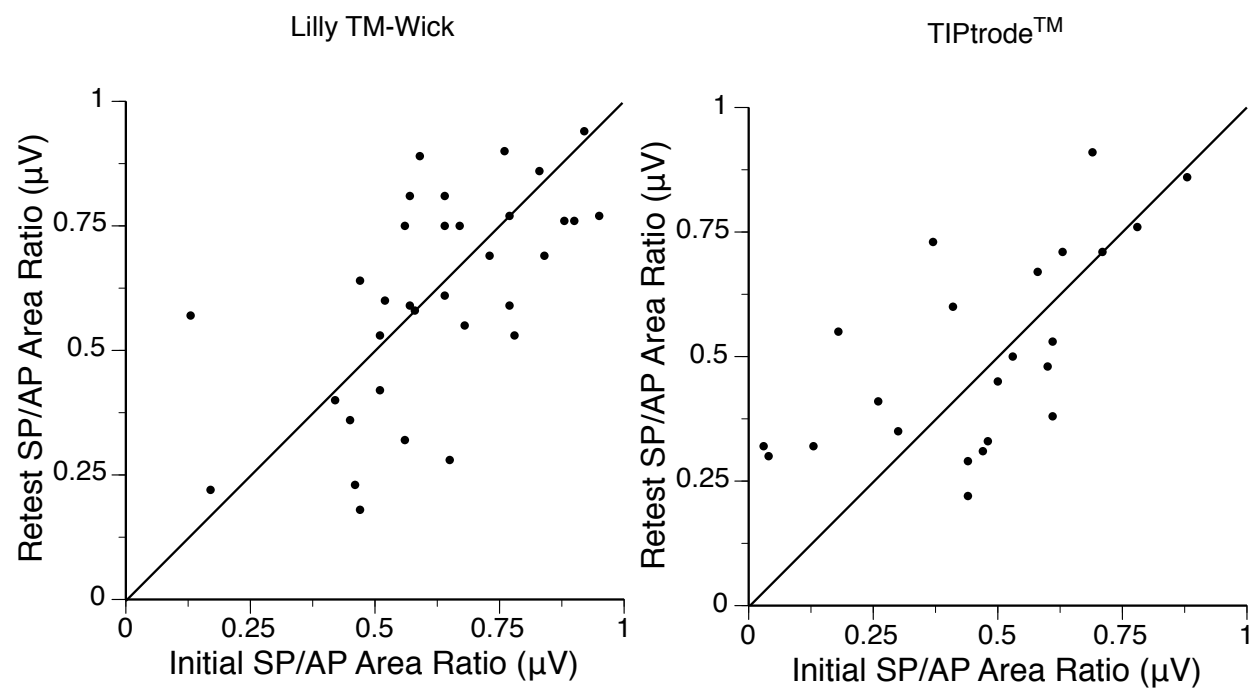


Figure 13. Bivariate scatter plots with line of equality of SP/AP amplitude ratio (μV) for initial test and retest as a function of electrode.



*Figure 14.* Bivariate scatter plots with line of equality of SP/AP area ratio ( $\mu\text{V}$ ) for initial test and retest as a function of electrode.

Finally, Bland-Altman plots (Bland & Altman, 1986, 1999) were constructed to examine reliability between the initial and subsequent tests for all the five ECoG indices for both electrode types and two rates. Each Bland–Altman plot is a bivariate scatterplot of the difference of two test measurements on the Y-axis and the average of the two test measurements on the X-axis. Superimposed on each plot are three horizontal reference lines. They include the average difference between the two test measurements (i.e., termed the bias) and the 95% limits of agreement (i.e., the mean difference  $\pm 1.96 SD$ ). Systematic bias/linear trend was explored examining the differences of two test measurements with linear regression.

### **SP Amplitude**

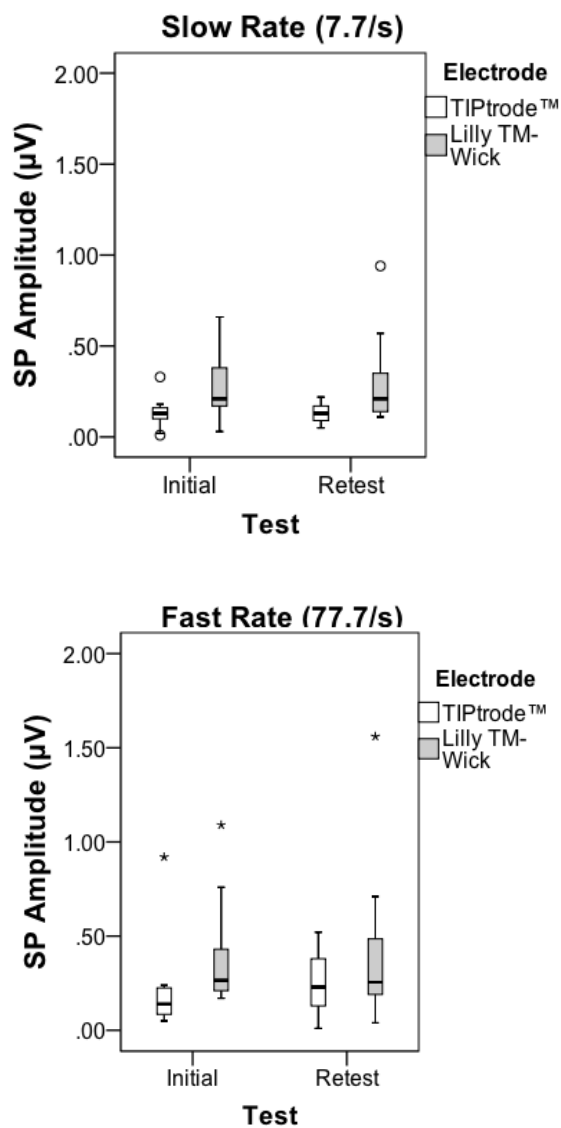
Mean and standard deviations for SP amplitudes as a function of test, rate, and electrode are shown in Table 4. Boxplots (Figure 15) were also constructed to visualize data and check the assumption of normalcy. A number of outliers were observed. These data points were retained in the inferential analysis that followed. A three-factor linear mixed model repeated measures ANOVA was conducted to examine SP amplitude differences as a function of test, rate, and electrode. The ANOVA summary for SP amplitude is presented in Table 5. Statistically significant main effects of electrode ( $p < .001$ ) and rate ( $p < .05$ ) were found. SP amplitudes were significantly larger for Lilly TM-Wick electrodes than for TIPtrodes™ and for the faster rate of 77.7/s than for the slower rate of 7.7/s. There were no other significant main effects or interactions.

Boxplots of SP amplitude differences as a function of rate and electrode are shown in Figure 16. The five number summary of the boxplot values is presented in

Table 4. *Mean SP Amplitudes ( $\mu\text{V}$ ) and Standard Deviations as a Function of Test, Rate, and Electrode.*

Electrode	Rate	Test	
		Initial	Retest
Lilly TM-Wick			
	7.7/s	0.28	0.29
		(0.17)	(0.21)
	<i>N</i>	18	17
	77.7/s	0.37	0.38
		(0.25)	(0.37)
	<i>N</i>	16	16
TIPtrode™			
	7.7/s	0.13	0.12
		(0.07)	(0.05)
	<i>N</i>	17	17
	77.7/s	0.23	0.25
		(0.28)	(0.16)
	<i>N</i>	8	10

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

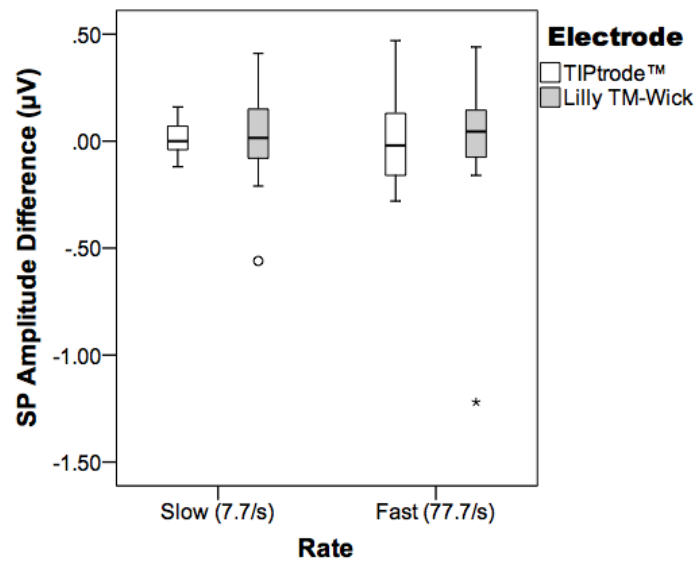


*Figure 15.* Boxplots of SP amplitude as a function of test, rate, and electrode. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

Table 5. *Summary of Three-Factor Linear Mixed Model Repeated Measures ANOVA Comparing Differences Between SP Amplitudes (in  $\mu\text{V}$ ) as a Function of Test (i.e., initial and retest), Electrode (i.e., Lilly TM-Wick and TIPTrode™), and Rate (i.e., 7.7/s and 77.7/s).*

Source	Numerator <i>df</i>	Denominator <i>df</i>	F	<i>p</i>
Test	1	65.66	0.02	.89
Electrode	1	107.20	17.82	<.001*
Rate	1	55.22	8.55	.01*

*Note.* *N* = 18 for ANOVA; \*statistically significant at  $p < .05$ . A fixed factorial model was first utilized and all interactions were not statistically significant ( $p > .05$ ). The analysis was then repeated with a fixed main effects model with the same findings as reported in this table.



*Figure 16.* Boxplots of SP amplitude differences as a function of rate and electrode. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).



Table 6. Mean and standard deviations for SP amplitude differences (i.e., initial test – retest) as a function of rate and electrode are shown in Table 7. Also contained in the table are the 95% confidence intervals of the mean differences. As evident in Table 7, all confidence intervals contain 0. This is additional evidence that the effect of test is not statistically significant and SP amplitude measures across tests are reliable.

The Bland-Altman plots for SP amplitude as a function of electrode and rate are shown in Figure 17. Two observations are evident in these plots: The 95% limits of agreement are larger for the Lilly TM-Wick electrode and the fast stimulus rate. There was no systematic variation with the mean differences of the two measurements evidenced by no linear predictive relationships between averaged and difference scores in any plots.

### **Effects of AP Latency**

Mean and standard deviations for AP latencies as a function of test, rate, and electrode are shown in Table 8. Boxplots (Figure 18) were also constructed to visualize data and check the assumption of normalcy. A number of outliers were observed. These data points were retained in the inferential analysis that followed. A three-factor linear mixed model repeated measures analysis of variance was conducted to examine AP latency differences as a function of test, rate, and electrode. The ANOVA summary for AP latency is presented in Table 9. A statistically significant main effect of rate ( $p < .001$ ) was found. AP latencies were significantly longer for the faster rate of 77.7/s than for the slow rate of 7.7/s. There were no other significant main effects or interactions.

Boxplots of AP latency differences as a function of rate and electrode are shown in Figure 19. The five number summary of the boxplot values is presented in Table 10.

Table 6. *Five Number Summary for Boxplots of SP Amplitude Differences as a Function of Rate and Electrode.*

Quantiles	Electrode			
	Lilly TM-Wick		TIPtrode™	
	Slow	Fast	Slow	Fast
Maximum	0.41	0.44	0.16	0.47
75%	0.14	0.15	0.08	0.22
50%	-0.01	0.04	0.00	-0.02
25%	-0.11	-0.10	-0.05	-0.19
Minimum	-0.56	-1.22	-0.12	-0.28

Table 7. Mean SP Amplitude Differences ( $\mu\text{V}$ ) and Standard Deviations as a Function of Rate and Electrode.

Electrode	Rate	SP Amplitude Difference	95% Confidence Interval	
			Lower Bound	Upper Bound
Lilly TM-Wick				
	7.7/s	0.00 (0.21)	-0.11	0.11
	<i>N</i>	17		
	77.7/s	-0.01 (0.36)	-0.20	0.18
	<i>N</i>	16		
TIPtrode™				
	7.7/s	0.00 (0.08)	-0.03	0.04
	<i>N</i>	17		
	77.7/s	0.02 (0.26)	-0.25	0.29
	<i>N</i>	6		

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

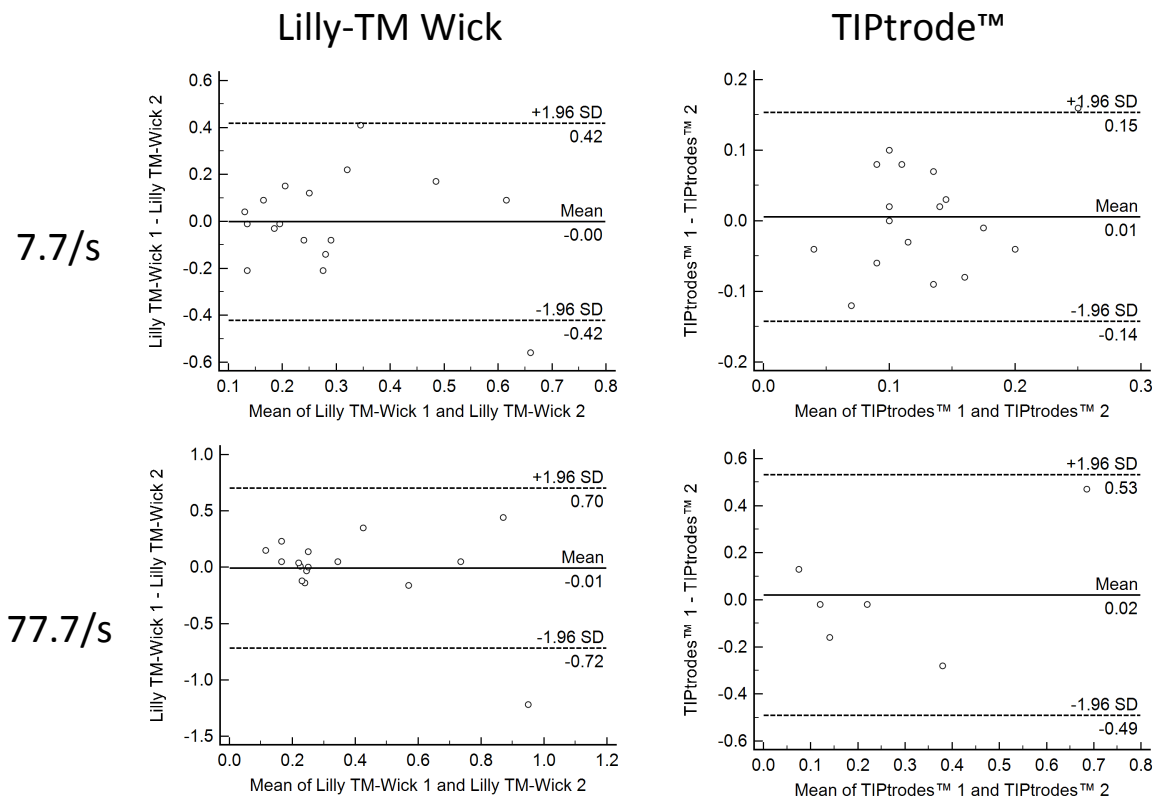
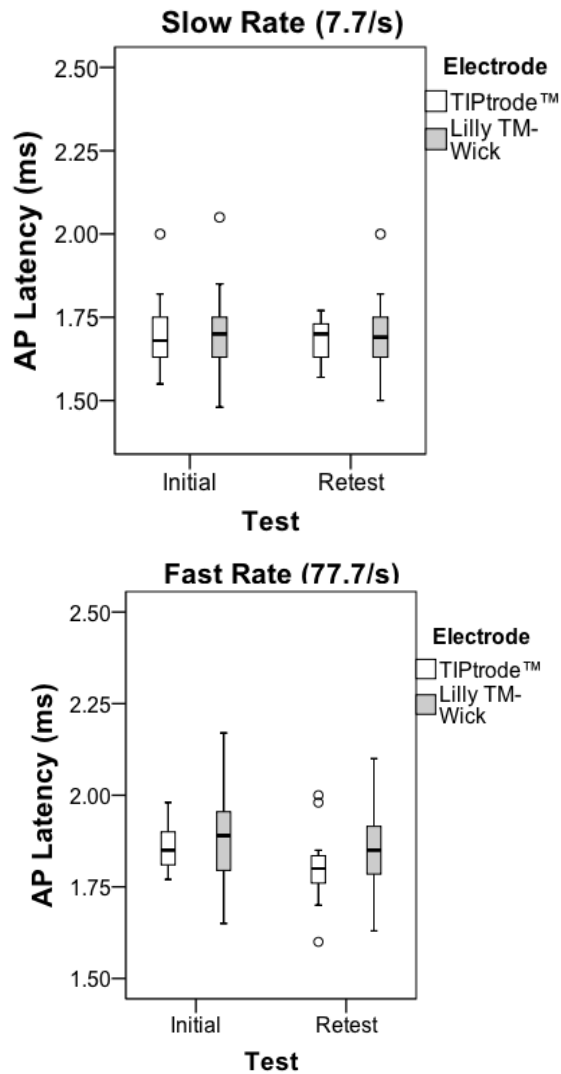


Figure 17. Bland-Altman plots for SP amplitude as a function of electrode and rate.

Table 8. *Mean AP Latencies (ms) and Standard Deviations as a Function of Test, Rate, and Electrode.*

Electrode	Rate	Test	
		Initial	Retest
Lilly-TM Wick			
	7.7/s	1.71	1.70
		(0.13)	(0.11)
	<i>N</i>	18	18
	77.7/s	1.89	1.86
		(0.14)	(0.12)
	<i>N</i>	16	16
TIPtrode™			
	7.7	1.70	1.68
		(0.11)	(0.07)
	<i>N</i>	17	17
	77.7	1.86	1.80
		(0.07)	(0.11)
	<i>N</i>	8	11

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

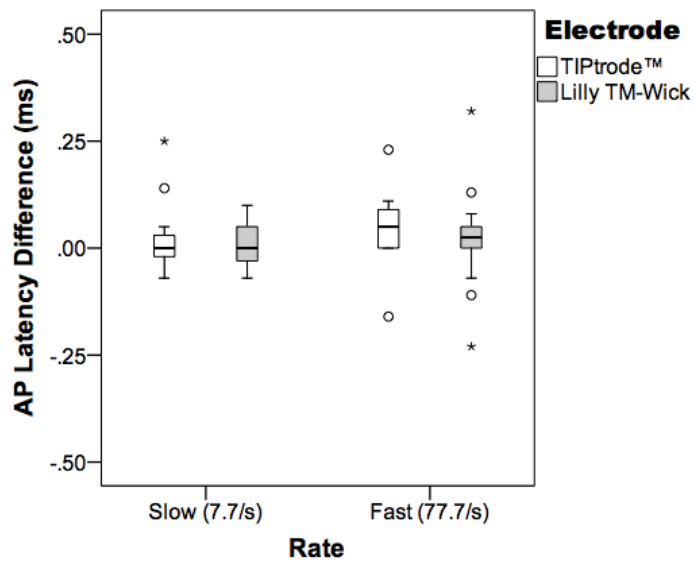


*Figure 18.* Boxplots of AP latency as a function of test, rate, and electrode. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range).

Table 9. *Summary of Three-Factor Linear Mixed Model Repeated Measures ANOVA Comparing Differences Between AP Latencies (in ms) as a Function of Test (i.e., initial and retest), Electrode (i.e., Lilly TM-Wick and TIPtrode™), and Rate (7.7/s and 77.7/s).*

Source	Numerator <i>df</i>	Denominator <i>df</i>	F	<i>p</i>
Test	1	74.84	0.83	.37
Electrode	1	111.41	1.17	.28
Rate	1	74.21	147.81	<.001*

*Note.* *N* = 18 for ANOVA; \*statistically significant at  $p < .05$ . A fixed factorial model was first utilized and all interactions were not statistically significant ( $p > .05$ ). The analysis was then repeated with a fixed main effects model with the same findings as reported in this table.



*Figure 19.* Boxplots of AP latency differences as a function of rate and electrode. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).



Table 10. *Five Number Summary for Boxplots of AP Latency Differences as a Function of Rate and Electrode.*

Quantiles	Electrode			
	Lilly TM-Wick		TIPtrode™	
	Slow	Fast	Slow	Fast
Maximum	0.10	0.32	0.25	0.23
75%	0.05	0.05	0.03	0.11
50%	0.00	0.02	0.00	0.05
25%	-0.37	0.00	-0.02	0.00
Minimum	-0.07	-0.23	-0.07	-0.16

Mean and standard deviations for AP latency differences (i.e., initial test – retest) as a function of rate and electrode are shown in Table 11. Also contained in the table are the 95% confidence intervals of the mean differences. As evident in Table 11, all confidence intervals contain 0. This is additional evidence that the effect of test is not statistically significant and AP latency measures across tests are reliable.

The Bland-Altman plots for AP latency as a function of electrode and rate are shown in Figure 20. The 95% limits of agreement are very similar between the two electrodes and across the two stimulus rates. There was no systematic variation with the mean differences of the two measurements evidenced by no linear predictive relationships between averaged and difference scores in any plots except for the TIPtrodes™ Test 1 and 2. When the outlier in this plot was removed from the analyses, the linear regression was not statistically significant.

### **Effects of AP Amplitude**

Mean and standard deviations for AP amplitude as a function of test, rate, and electrode are shown in Table 12. Boxplots (Figure 21) were also constructed to visualize data and check the assumption of normalcy. A number of outliers were observed. These data points were retained in the inferential analysis that followed. A three-factor linear mixed model repeated measures analysis of variance was conducted to examine AP amplitude differences as a function of test, rate, and electrode. The ANOVA summary for AP amplitude is presented in Table 13. Statistically significant main effects of electrode ( $p < .001$ ) and rate ( $p < .05$ ) were found. AP amplitudes were significantly larger for Lilly TM-Wick electrodes than TIPtrodes™ and for the slower rate

Table 11. *Mean AP Latency Differences (ms) and Standard Deviations as a Function of Rate and Electrode.*

Electrode	Rate	AP Latency Difference	95% Confidence Interval	
			Lower Bound	Upper Bound
Lilly TM-Wick				
	7.7/s	0.01 (0.05)	-0.02	0.04
	<i>N</i>	18		
	77.7/s	0.02 (0.11)	-0.04	0.08
	<i>N</i>	16		
TIPtrode™				
	7.7/s	0.02 (0.07)	-0.02	0.06
	<i>N</i>	17		
	77.7/s	0.04 (0.12)	-0.07	0.15
	<i>N</i>	7		

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

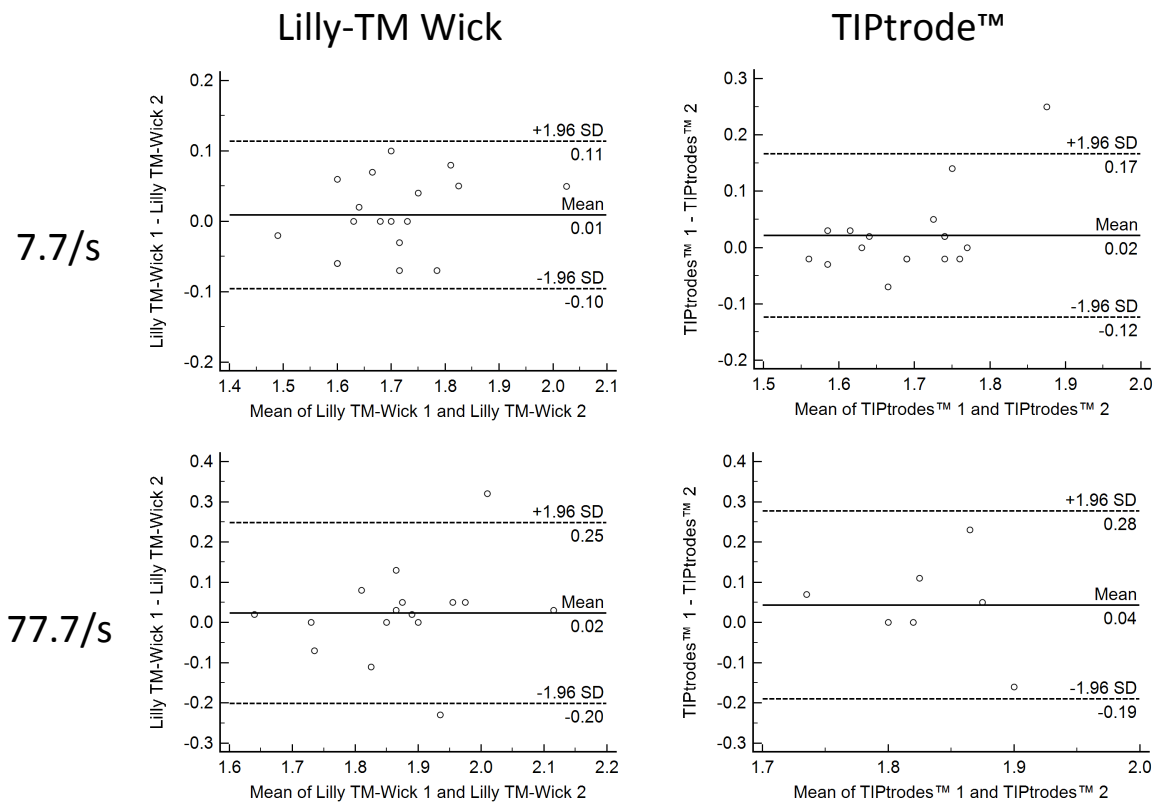


Figure 20. Bland-Altman plots for AP latency as a function of electrode and rate.

Table 12. *Mean AP Amplitudes ( $\mu$ V) and Standard Deviations as a Function of Test, Rate, and Electrode.*

Electrode	Rate	Test	
		Initial	Retest
Lilly-TM Wick			
	7.7/s	0.87	1.02
		(0.37)	(0.59)
	<i>N</i>	18	18
	77.7	0.76	0.75
		(0.45)	(0.53)
	<i>N</i>	16	16
TIPtrode™			
	7.7/s	0.50	0.51
		(0.18)	(0.17)
	<i>N</i>	17	17
	77.7/s	0.52	0.43
		(0.41)	(0.26)
	<i>N</i>	8	11

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

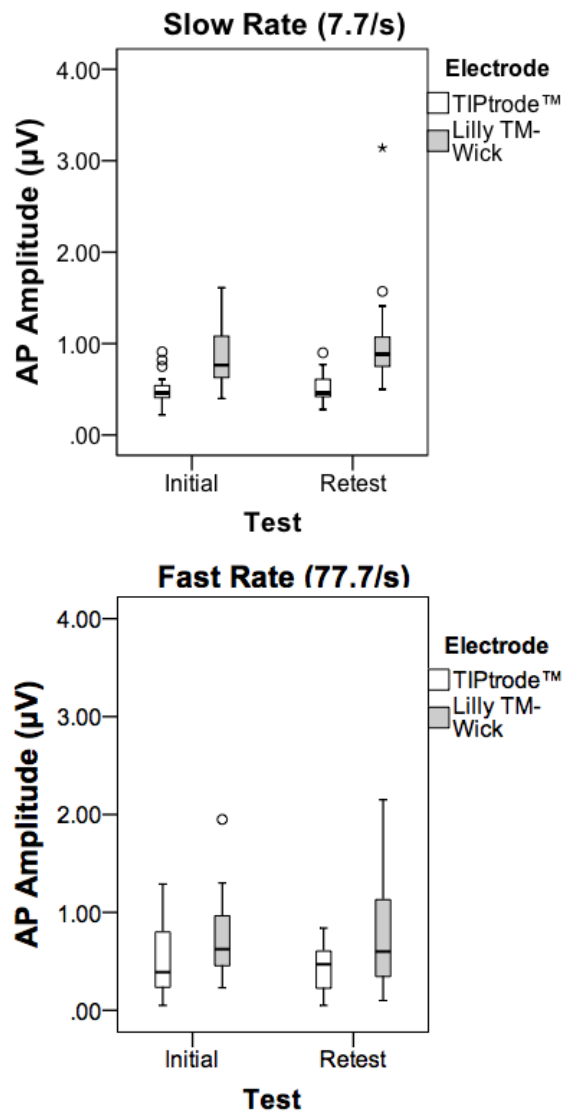


Figure 21. Boxplots of AP amplitude as a function of test, rate, and electrode. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

Table 13. *Summary of Three-Factor Linear Mixed Model Repeated Measures ANOVA Comparing Differences Between AP Amplitudes (in  $\mu V$ ) as a Function of Test (i.e., initial and retest), Electrode (i.e., Lilly TM-Wick and TIPtrode™), and Rate (i.e., 7.7/s and 77.7/s).*

Source	Numerator <i>df</i>	Denominator <i>df</i>	F	<i>p</i>
Test	1	79.35	0.05	.82
Electrode	1	112.72	35.74	<.001*
Rate	1	81.18	6.52	.01*

*Note.* *N* = 18 for ANOVA; \*statistically significant at  $p < .05$ . A fixed factorial model was first utilized and all interactions were not statistically significant ( $p > .05$ ). The analysis was then repeated with a fixed main effects model with the same findings as reported in this table.

of 7.7/s than for the faster rate of 77.7/s. There were no other significant main effects or interactions.

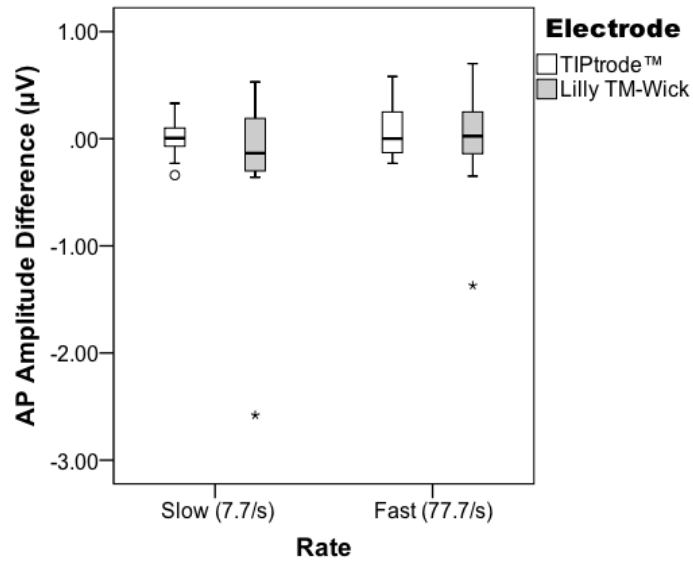
Boxplots of AP amplitude differences as a function of rate and electrode are shown in Figure 22. The five number summary of the boxplot values is presented in Table 14. Mean and standard deviations for AP amplitude differences (i.e., initial test – retest) as a function of rate and electrode are shown in Table 15. Also contained in the table are the 95% confidence intervals of the mean differences. As evident in Table 15, all confidence intervals contain 0. This is additional evidence that the effect of test is not statistically significant and AP amplitude measures across tests are reliable.

The Bland-Altman plots for AP amplitude as a function of electrode and rate are shown in Figure 23. As with SP amplitude, AP amplitude 95% limits of agreement are much larger with the Lilly TM-Wick electrode. There was no systematic variation with the mean differences of the two measurements evidenced by no linear predictive relationships between averaged and difference scores in any plots.

### **Effects of SP/AP Amplitude Ratio**

Mean and standard deviations for SP/AP amplitude ratio as a function of test, rate, and electrode are shown in Table 16. Boxplots (Figure 24) were also constructed to visualize data and check the assumption of normalcy. A number of outliers were observed. These data points were retained in the inferential analysis that followed. A three-factor linear mixed model repeated measures analysis of variance was conducted to examine SP/AP amplitude ratio differences as a function of test, rate, and electrode. The ANOVA summary for SP/AP amplitude ratio is presented in Table 17. A statistically





*Figure 22.* Boxplots of AP amplitude differences as a function of rate and electrode. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

Table 14. *Five Number Summary for Boxplots of AP Amplitude Differences as a Function of Rate and Electrode.*

Quantiles	Electrode			
	Lilly TM-Wick		TIPtrode™	
	Slow	Fast	Slow	Fast
Maximum	0.53	0.32	0.33	0.58
75%	0.19	0.05	0.10	0.28
50%	-0.14	0.02	0.01	0.00
25%	-0.30	0.00	-0.10	-0.21
Minimum	-2.58	-0.23	-0.34	-0.23

Table 15. Mean AP Amplitudes Differences ( $\mu V$ ) and Standard Deviations as a Function of Rate and Electrode.

			95% Confidence Interval	
Electrode	Rate	AP Amplitude Difference	Lower Bound	Upper Bound
Lilly TM-Wick				
	7.7/s	-0.15 (0.67)	-0.48	0.18
	<i>N</i>	18		
	77.7/s	0.02 (0.11)	-0.04	0.08
	<i>N</i>	16		
TIPtrode™				
	7.7/s	0.00 (0.16)	-0.09	0.08
	<i>N</i>	17		
	77.7/s	0.08 (0.29)	-0.19	0.36
	<i>N</i>	7		

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

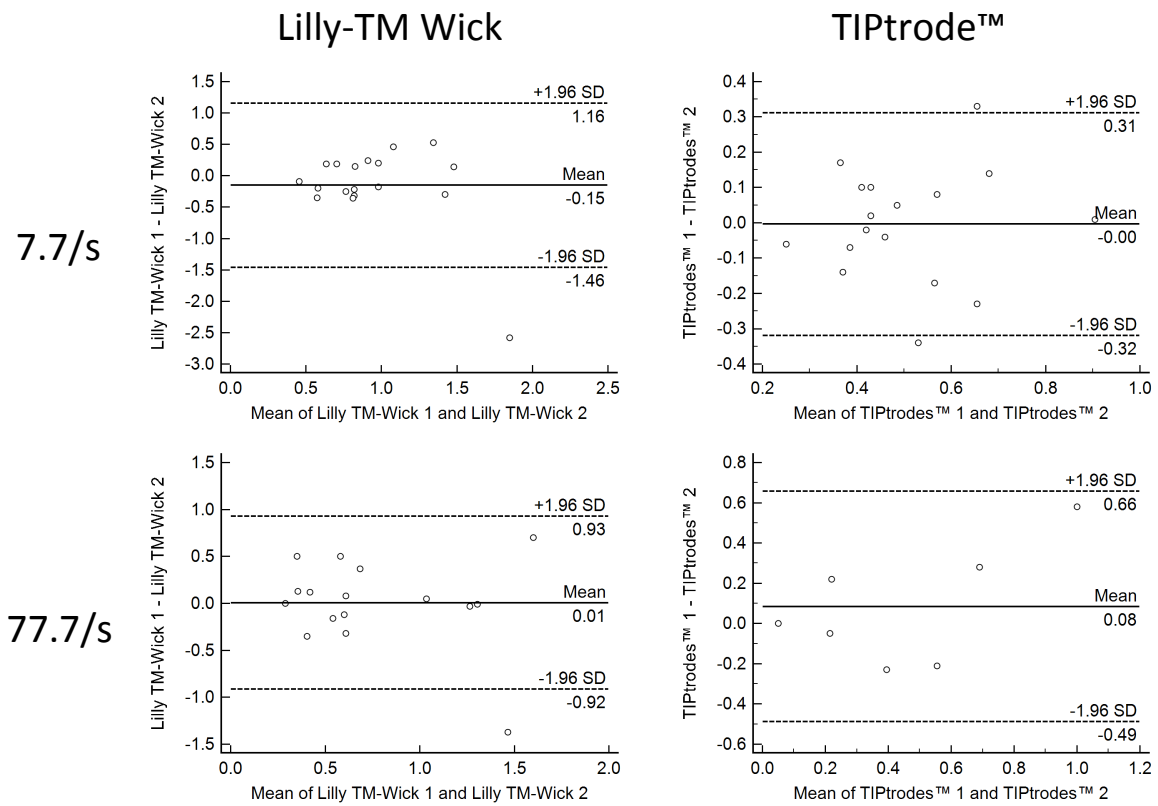


Figure 23. Bland-Altman plots for AP amplitude as a function of electrode and rate.

Table 16. Mean SP/AP Amplitude Ratios ( $\mu\text{V}$ ) and Standard Deviations as a Function of Test, Rate, and Electrode.

Electrode	Rate	Test	
		Initial	Retest
Lilly-TM Wick			
	7.7/s	0.32	0.32
		(0.14)	(0.15)
	<i>N</i>	18	17
	77.7/s	0.51	0.47
		(0.17)	(0.18)
	<i>N</i>	16	16
TIPtrode™			
	7.7/s	0.26	0.25
		(0.12)	(0.11)
	<i>N</i>	17	17
	77.7/s	0.49	0.48
		(0.28)	(0.20)
	<i>N</i>	8	10

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

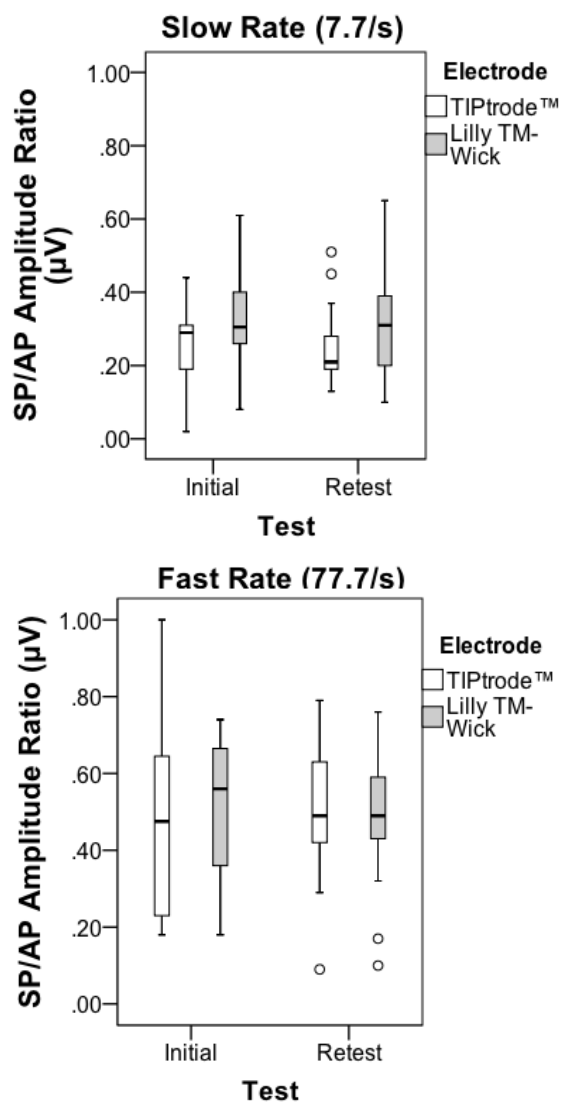


Figure 24. Boxplots of SP/AP amplitude ratio as a function of test, rate, and electrode.

The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

Table 17. *Summary of Three-Factor Linear Mixed Model Repeated Measures ANOVA Comparing Differences Between SP/AP Amplitude Ratio (in  $\mu\text{V}$ ) as a Function of Test (i.e., initial and retest), Electrode (i.e., Lilly TM-Wick and TIPtrode™), and Rate (i.e., 7.7/s and 77.7/s).*

Source	Numerator <i>df</i>	Denominator <i>df</i>	F	<i>p</i>
Test	1	77.31	0.25	.62
Electrode	1	109.58	3.77	.06
Rate	1	68.28	73.95	<.001*

*Note.* *N* = 18 for ANOVA; \*statistically significant at  $p < .05$ . A fixed factorial model was first utilized and all interactions were not statistically significant ( $p > .05$ ). The analysis was then repeated with a fixed main effects model with the same findings as reported in this table.

significant main effect of rate ( $p < .001$ ) was found. SP/AP amplitude ratios were significantly larger for the faster rate of 77.7/s than for the slower rate of 7.7/s. There were no other significant main effects or interactions.

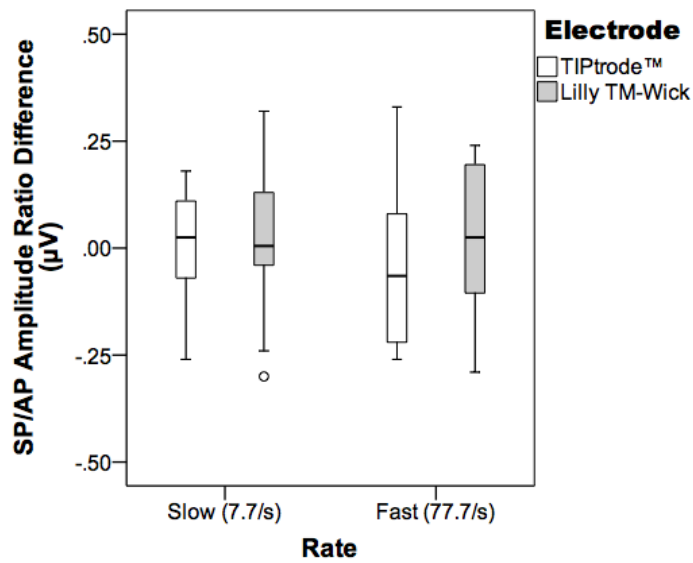
Boxplots of SP/AP amplitude ratio differences as a function of rate and electrode are shown in Figure 25. The five number summary of the boxplot values is presented in Table 18. Mean and standard deviations for SP/AP amplitude ratio differences (i.e., initial test – retest) as a function of rate and electrode are shown in Table 19. Also contained in the table are the 95% confidence intervals of the mean differences. As evident in Table 19, all confidence intervals contain 0. This is additional evidence that the effect of test is not statistically significant and SP/AP amplitude ratio measures across tests are reliable.

The Bland-Altman plots for SP/AP amplitude ratio as a function of electrode and rate are shown in Figure 26. The SP/AP amplitude ratio 95% limits of agreement are similar between the two electrodes and stimulus rates. There was no systematic variation with the mean differences of the two measurements evidenced by no linear predictive relationships between averaged and difference scores in any plots.

### **Effects of SP/AP Area Ratio**

Mean and standard deviations for SP/AP area ratio as a function of test, rate, and electrode are shown in Table 20. Boxplots (Figure 27) were also constructed to visualize data and check the assumption of normalcy. A number of outliers were observed. These data points were retained in the inferential analysis that followed. A three-factor linear mixed model repeated measures analysis of variance was conducted





*Figure 25.* Boxplots of SP/AP amplitude ratio differences as a function of rate and electrode. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

Table 18. *Five Number Summary for Boxplots of SP/AP Amplitude Ratio Differences as a Function of Rate and Electrode.*

Quantiles	Electrode			
	Lilly TM-Wick		TIPtrode™	
	Slow	Fast	Slow	Fast
Maximum	0.26	0.24	0.18	0.33
75%	0.12	0.20	0.12	0.14
50%	0.00	0.02	0.04	-0.06
25%	-0.06	-0.11	-0.09	-0.23
Minimum	-0.30	-0.29	-0.26	-0.26

Table 19. Mean SP/AP Amplitude Ratio Differences ( $\mu\text{V}$ ) and Standard Deviations as a Function of Rate and Electrode.

			95% Confidence Interval	
Electrode	Rate	SP/AP Amplitude Ratio	Lower	Upper
		Difference	Bound	Bound
Lilly TM-				
Wick	7.7/s	0.01	-0.07	0.08
		(0.15)		
	<i>N</i>	17		
	77.7/s	0.02	-0.06	0.11
		(0.17)		
	<i>N</i>	16		
TlPtrode™				
	7.7/s	0.01	-0.05	0.08
		(0.13)		
	<i>N</i>	17		
	77.7/s	-.033	-.027	0.20
		(.23)		
	<i>N</i>	6		

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

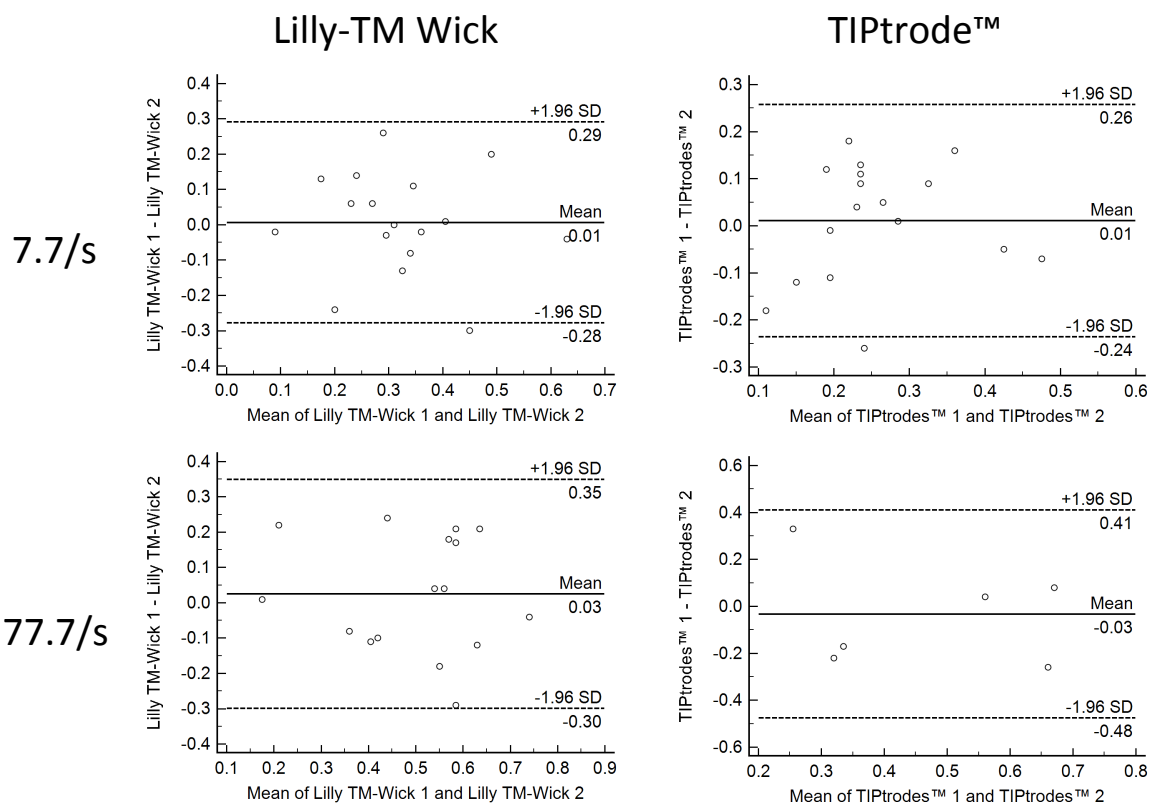
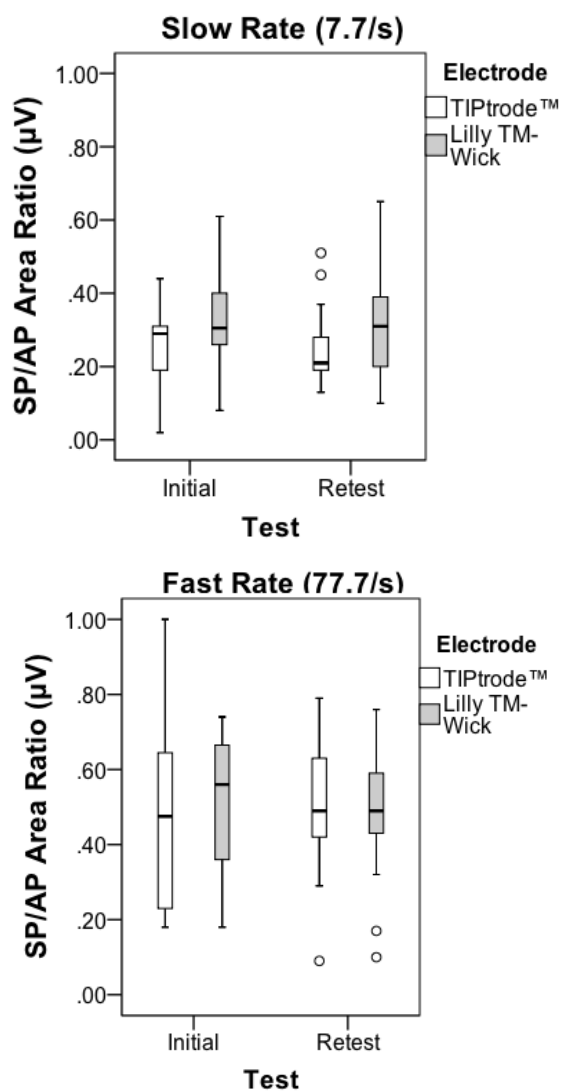


Figure 26. Bland-Altman plots for SP/AP amplitude ratio as a function of electrode and rate.

Table 20. Mean SP/AP Area Ratios ( $\mu\text{V}$ ) and Standard Deviations as a Function of Test, Rate, and Electrode.

Electrode	Rate	Test	
		Initial	Retest
Lilly-TM Wick			
	7.7/s	0.54	0.52
		(0.17)	(0.19)
	<i>N</i>	18	17
	77.7/s	0.72	0.71
		(0.16)	(0.19)
	<i>N</i>	16	16
TIPtrode™			
	7.7/s	0.40	0.42
		(0.20)	(0.14)
	<i>N</i>	17	17
	77.7/s	0.64	0.70
		(0.26)	(0.15)
	<i>N</i>	8	10

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.



*Figure 27.* Boxplots of SP/AP area ratio as a function of test, rate, and electrode. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

to examine SP/AP area ratio differences as a function of test, rate, and electrode. The ANOVA summary for SP/AP area ratio is presented in Table 21. Statistically significant main effects of electrode ( $p < .05$ ) and rate ( $p < .001$ ) were found. SP/AP area ratios were significantly larger for Lilly TM-Wick electrode recordings than for TIPtrode™ recordings and for the faster rate of 77.7/s than for the slower rate of 7.7/s. There were no other significant main effects or interactions.

Boxplots of SP/AP area differences as a function of rate and electrode are shown in Figure 28. The five number summary of the boxplot values is presented in Table 22. Mean and standard deviations for SP/AP area ratio differences (i.e., initial test – retest) as a function of rate and electrode are shown in Table 23. Also contained in the table are the 95% confidence intervals of the mean differences. As evident in Table 23, all confidence intervals contain 0. This is additional evidence that the effect of test is not statistically significant and SP/AP area ratio measures across tests are reliable.

The Bland-Altman plots for SP/AP area ratio as a function of electrode and rate are shown in Figure 29. The SP/AP area ratio 95% limits of agreement were similar between the two electrodes at the slow stimulus rate. At the fast rate, however, the Lilly TM-Wick had a much larger 95% limits of agreement versus the TIPtrode™.electrode. There was no systematic variation with the mean differences of the two measurements evidenced by no linear predictive relationships between averaged and difference scores in any plots.

## **Discussion**

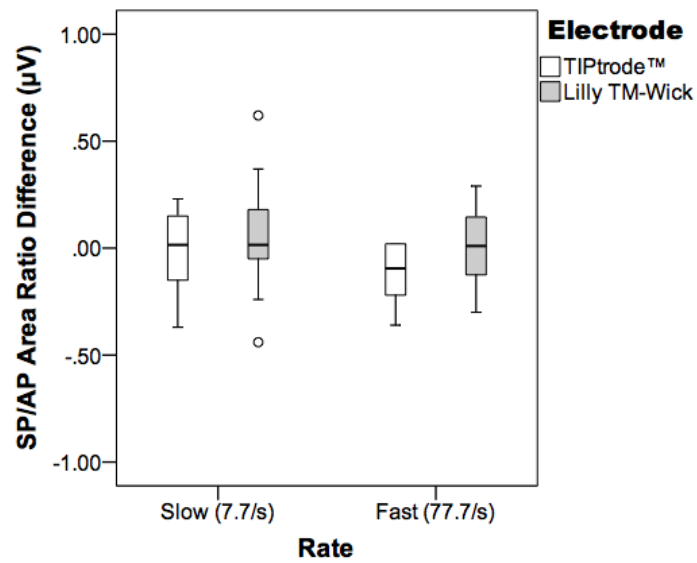
The aim of the first experiment was to examine the test-retest reliability of ECoG while using two electrode types and two stimulus rates. This is the first report

Table 21. *Summary of Three-Factor Linear Mixed Model Repeated Measures ANOVA Comparing Differences Between SP/AP Area Ratio (in  $\mu\text{V}$ ) as a Function of Test (i.e., initial and retest), Electrode (i.e., Lilly TM-Wick and TIPtrode™), and Rate (i.e., 7.7/s and 77.7/s)*

Source	Numerator <i>df</i>	Denominator <i>df</i>	F	<i>p</i>
Test	1	74.04	0.00	.97
Electrode	1	108.20	10.80	.001*
Rate	1	68.94	78.44	<.001*

*Note.* *N* = 18 for ANOVA; \*statistically significant at  $p < .05$ . A fixed factorial model was first utilized and all interactions were not statistically significant ( $p > .05$ ). The analysis was then repeated with a fixed main effects model with the same findings as reported in this table.





*Figure 28.* Boxplots of SP/AP area ratio differences as a function of rate and electrode.

The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

Table 22. *Five Number Summary for Boxplots of SP/AP Area Ratio Differences as a Function of Rate and Electrode.*

Quantiles	Electrode			
	Lilly TM-Wick		TIPtrode™	
	Slow	Fast	Slow	Fast
Maximum	0.37	0.29	0.23	0.02
75%	0.16	0.15	0.15	0.02
50%	0.00	0.01	0.03	-0.10
25%	-0.06	-0.13	-0.17	-0.26
Minimum	-0.44	-0.30	-0.37	-0.36

Table 23. Mean SP/AP Area Ratio Differences ( $\mu V$ ) and Standard Deviations as a Function of Rate and Electrode.

			95% Confidence Interval	
Electrode	Rate	SP/AP Area Ratio Difference	Lower Bound	Upper Bound
Lilly TM-Wick				
	7.7/s	0.02	-0.08	0.12
		(0.19)		
	<i>N</i>	17		
	77.7/s	0.01	-0.08	0.10
		(0.17)		
	<i>N</i>	16		
TIPtrode™				
	7.7/s	-0.02	-0.11	0.08
		(0.19)		
	<i>N</i>	17		
	77.7/s	-0.12	-0.29	0.04
		(0.16)		
	<i>N</i>	6		

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

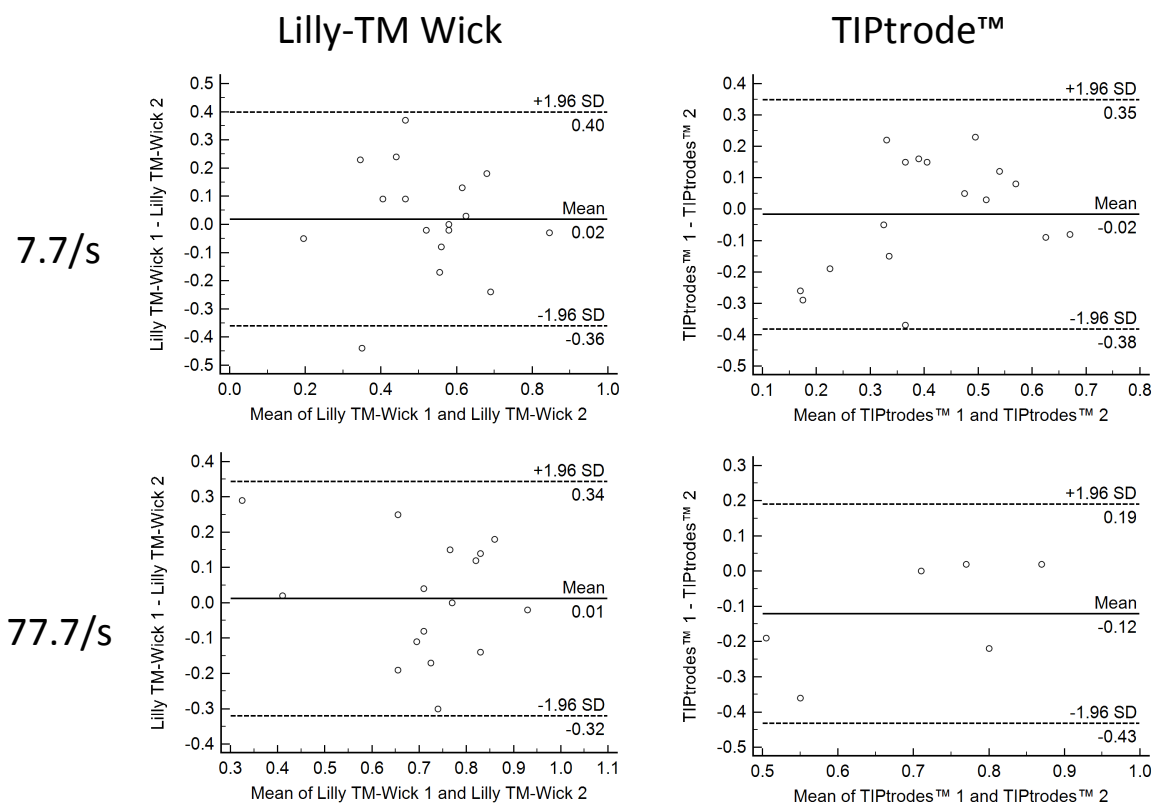


Figure 29. Bland-Altman plots for SP/AP area ratio as a function of electrode and rate.

of reliability of ECoChG indices including SP/AP area ratio recorded with extratympanic (TIPtrode™) and tympanic (Lilly TM-Wick) electrodes at slow (7.7/s) and fast (77.7/s) stimulus rates. Initially, the logistic regression analysis was utilized to examine the predictor values of test, electrode, and rate for response presence or absence. The findings from the initial analysis are consistent with the notion that ECoChG responses are more apt to be present when recorded with a Lilly TM-Wick electrode than a TIPtrode™ electrode and at a slower stimulus rate of 7.7/s than a faster rate of 77.7/s. Test was not a predictor value for presence or absence of response.

Traditionally, correlation coefficients ( $r$ ) have been used to examine the association between test-retest measures of auditory function. Statistically significant correlations between initial test and retest were found between ECoChG measures of SP amplitude, AP latency, AP amplitude, SP/AP amplitude ratio, and SP/AP area ratio when recorded with Lilly TM-Wick electrodes. Statistically significant correlations between initial test and retest were found between ECoChG measures of all ECoChG indices except for SP amplitude when recorded with TIPtrodes™. It is recognized that using a correlation together with a  $p$ -value for the null hypothesis of zero correlation has limitations as a measure of reliability. Consider a correlation of 1, which indicates the strongest possible correlation, where all pairs of values fall exactly along a line. This may be the case where all pairs having exactly the same value are indicative of perfect reliability. It could also be the case where, for example, a retest measure is double the test measure – a perfect correlation but hardly a reliable measurement. When the  $p$ -value indicates statistical significance, one must be cognizant this there is sufficient evidence in the sample to reject a claim that the test-retest values are

uncorrelated; however, it does not mean that differences of the test-retest pairs are small. For a test to be reliable these differences should be small on a clinically relevant scale.

Lilly TM-Wick electrodes resulted in larger SP amplitudes, AP amplitudes, and SP/AP area ratios than TIPTrode™ electrodes. These findings are similar to others with regards to SP and AP amplitudes (Ferraro, 2010; Ferraro & Krishnan, 1997; Ferraro et al., 1994; Lambert & Ruth, 1988). Main effects of rate were identified for SP amplitude, AP latency, AP amplitude, SP/AP amplitude ratio, and SP/AP area ratio. More specifically, AP latencies were longer for the faster rate, AP amplitudes were larger for the slower rate, and SP amplitudes, SP/AP amplitude ratios and SP/AP area ratios were larger for the faster rate. There were no main effects of test on any of the ECoChG indices.

The findings of Experiment 1 are consistent with the notion that ECoChG recordings with both electrode types (Lilly TM-Wick and TIPTrode™) are reliable tests to be used in assessment and reassessment of ECoChG indices. Mean differences between test and retest were near zero for all conditions tested. Additionally, 95% of the differences were less than  $\pm 1.96 SD$ . The magnitude of these bounds varied across electrode type, stimulus rate, and ECoChG indices as seen in Figures 17, 20, 23, 26, and 29. The magnitudes of these bounds were small enough that the measures were considered clinically reliable.

These results strongly support the notion that ECoChGs recorded with Lilly TM-Wick electrodes are superior to TIPTrode™ recordings due to the greater response presence and larger measured amplitudes. In addition, even though faster stimulus

rates result in an increased SP amplitude, results from this study are consistent with the notion that slower stimulus rates also allow for a greater response presence (Wilson & Bowker, 2002).

## CHAPTER III: EXPERIMENT 2 – THE EFFECT OF NOISE EXPOSURE ON BEHAVIORAL THRESHOLDS

It is well understood that noise exposure has an adverse impact on hearing sensitivity. A noise induced TTS has been characterized as a reduction in hearing sensitivity, a sensation of aural fullness due to the reduction in high-frequency hearing sensitivity, and tinnitus (Feuerstein & Chasin, 2009). It is also understood that the amount and duration of the noise induced TTS is dependent upon the duration and intensity of the noise. NIHL most often occurs bilaterally with the first sign being the classic notching of the audiogram between 3000 Hz and 6000 Hz with some degree of recovery at 8000 Hz (ACOEM, 2003; Dobie, 2005). When it comes to the susceptibility of one ear over the other to excessive noise exposure, research is equivocal. Pirilä (1991a, b) found that the average TTS following exposure to broadband noise presented at 91 dBA was significantly larger for the left ear than the right ear. Comparatively, Hooks-Horton et al. (2001) failed to find an ear effect on TTS resulting from exposure to a 2000 Hz narrowband noise presented at 102 dB SPL. It was suggested that this may be due to the differing noise stimuli utilized in each study. In addition, little is known with regards to the relationship between TTSs following noise exposure and acoustic reflex measures. The aim of this study was to examine the effects of noise exposure on behavioral thresholds and acoustic reflex indices including threshold and latency measures. Effects of gender and ear were also examined.



## Methods

### Participants

Sixteen adult males ranging in age from 21 to 30 years with a mean age of 25.4 ( $SD = 2.9$ ) years and 16 adult females ranging in age from 20 to 29 years with a mean age of 24.0 ( $SD = 2.4$ ) years served as participants for this study.<sup>1</sup> An independent samples  $t$ -test was utilized to examine whether there was a significant difference of age between males and females. The difference in age between males and females was not significant,  $t(30) = -1.52$ ,  $p = .138$ .

Participants were Caucasians with a negative history of loud noise exposure within 48 hours prior to data collection as per self-report. They also reported no significant history of neurological, otological, and/or communication disorders. Both ears were tested on each participant for a total of 32 ears. All participants had normal hearing sensitivity defined as pure tone thresholds at octave frequencies from 250 Hz to 8000 Hz  $\leq 15$  dB HL (American National Standards Institute, 2010). Mean audiometric thresholds for all participants as a function of frequency, ear, and gender are displayed in Table 24. Boxplots (Figure 30) were also constructed to visualize data and check the assumption of normalcy. As a rule of thumb, the ratio of the largest to smallest standard

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<sup>1</sup> For this and subsequent studies, the sample size ( $N \geq 16$ ) was calculated (*G\*Power*) by assuming a large effect ( $\eta_p^2 = .4$ ) and  $\phi$  of .80 to find a statistically significant effect of noise on auditory thresholds, DPOAE amplitudes, and ECoG indices with an  $\alpha$  of .05 (Cohen, 1988). The estimated large effect size was gleaned from Horton et al. (2001) for auditory threshold and DPOAE amplitude. For ECoG indices, effect size estimates came from Kim et al. (2005) and Nam and Wong (2004).

Table 24: *Mean Audiometric Thresholds (dB HL) as a Function of Frequency, Ear, and Gender.*

		Frequency (Hz)							
		250	500	1000	2000	3000	4000	6000	8000
Male (N=16)									
Ear									
	Right	10.6	10.6	8.8	6.6	6.9	4.4	1.9	-3.4
		(4.0)	(4.4)	(2.9)	(4.4)	(5.1)	(4.8)	(5.7)	(5.4)
	Left	10.0	10.6	8.4	7.8	6.3	4.7	2.5	-4.4
		(3.7)	(3.1)	(4.0)	(4.5)	(5.3)	(4.6)	(5.2)	(4.8)
Female (N=16)									
Ear									
	Right	9.1	7.5	7.5	6.3	4.4	2.8	1.3	-4.1
		(3.8)	(4.8)	(4.8)	(3.9)	(4.4)	(5.2)	(5.3)	(6.1)
	Left	7.5	6.9	5.0	4.1	3.4	1.3	1.3	-3.4
		(4.1)	(3.6)	(5.2)	(5.2)	(6.5)	(5.6)	(6.5)	(6.3)

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

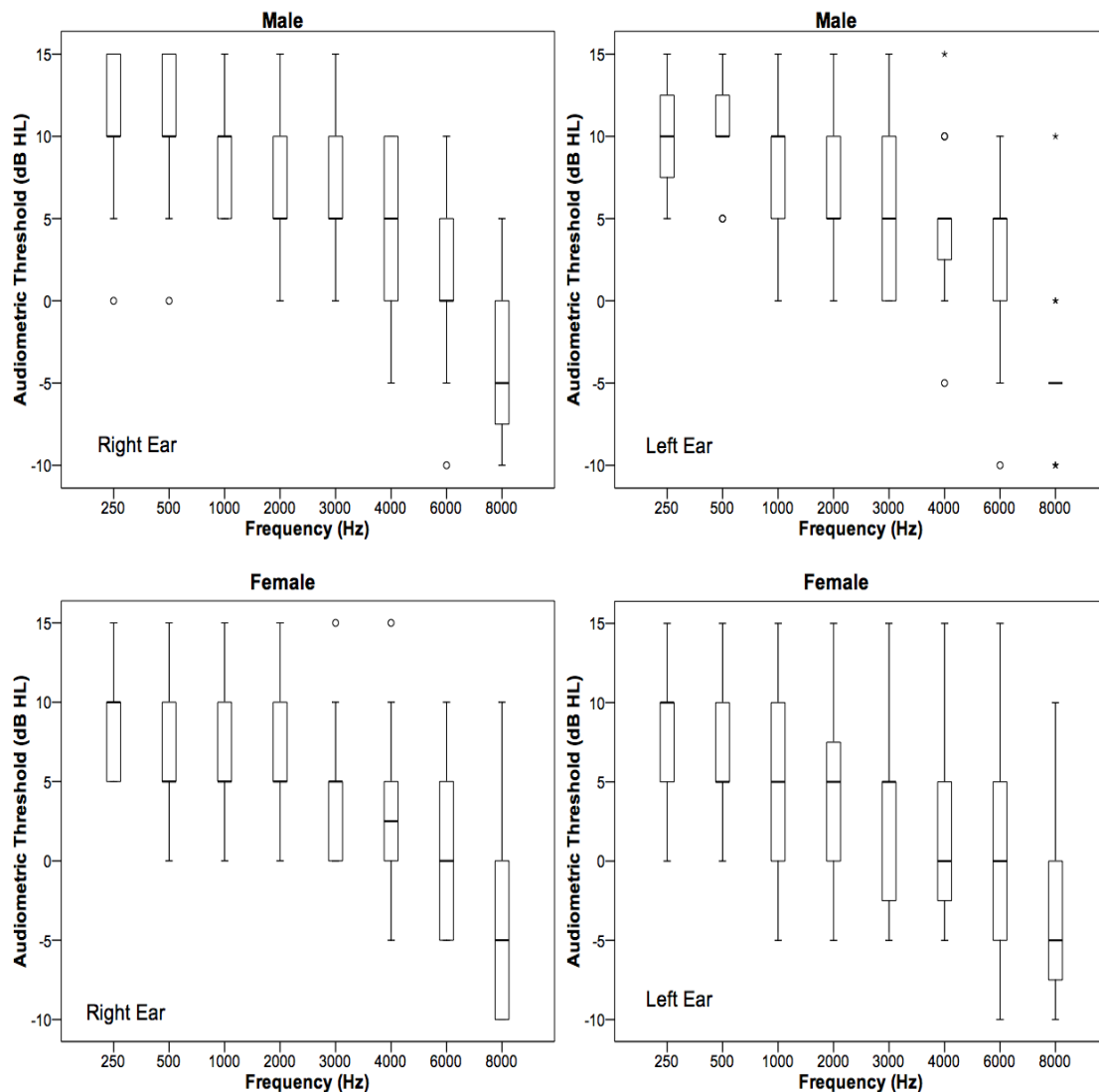


Figure 30. Boxplots of audiometric thresholds as a function of gender and ear. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

deviation should be less than 2. In the case of boxplots, the length of one box (i.e., the interquartile range which is a measure of spread) should not be more than twice the length of the other box. A three-factor mixed repeated measures ANOVA was conducted to examine baseline behavioral thresholds as a function of frequency, ear, and gender. The ANOVA summary is shown in Table 25. Mauchly's Test of Sphericity was used to test the compound symmetry assumption. For instances in which Mauchly's test indicated that the sphericity condition was not satisfied, the degrees of freedom and  $p$  values were adjusted and Greenhouse-Geisser values were reported instead. There was a main effect of frequency ( $p < .0001$ ). No statistically significant main effects of ear or gender were seen ( $p > .05$ ) and no statistically significant two- or three- way interactions were found.

Participants also had normal middle ear function defined as  $Y_{tm} = 0.3\text{-}1.50$  mmho,  $TW = 35.80\text{-}95.00$  daPa,  $V_{ea} = 0.9\text{-}1.80$  cm<sup>3</sup>, and  $TPP \pm 50$  daPa (Roup et al., 1998; Marshall, Heller, & Westhusin, 1997). Mean tympanometric indices for all participants as a function of ear and gender are displayed in Table 26. Boxplots (Figures 31 to 34) were also constructed to visualize data and check the assumption of normalcy. Four separate two-factor linear mixed model ANOVAs with repeated measures were performed to determine the effect of ear and gender on tympanometric indices including  $Y_{tm}$ ,  $TW$ ,  $TTP$ , and  $V_{ea}$  (see Tables 27 to 30). With regards to  $V_{ea}$ , a statistically significant main effect of gender was found. Mean  $V_{ea}$  was significantly larger for males than for females. There were no other significant main effects or interactions for any of the four tympanometric indices.

Table 25. *Summary of Three-Factor Mixed Measures ANOVA Comparing Differences Between Behavioral Thresholds (in dB HL) as a Function of Frequency, Ear, and Gender.*

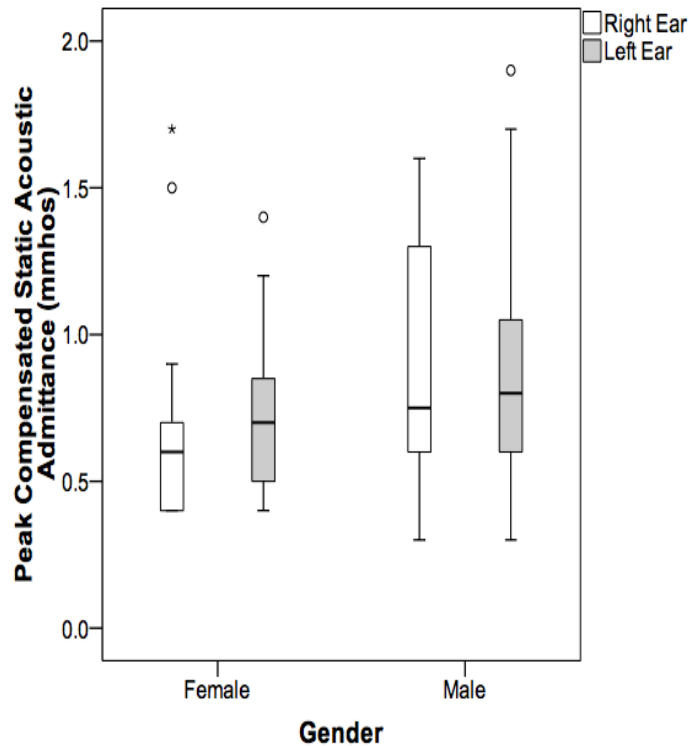
Source	Sum of Squares	<i>df</i>	Mean Square	<i>F</i>	<i>p</i>	$\eta_p^2$
Frequency	8465.19	4.78	1770.71	52.45	< .0001 <sup>*a</sup>	.64
Ear	41.06	1	41.06	3.11	.09	.09
Gender	498.10	1	498.10	3.81	.06	.11

*Note.* *N* = 32 for ANOVA; \*statistically significant at  $p < .05$ ; <sup>a</sup>Greenhouse-Geisser value. A fixed factorial model was first utilized and all interactions were not statistically significant ( $p > .05$ ). The analysis was then repeated with a fixed main effects model with the same findings as reported in this table.

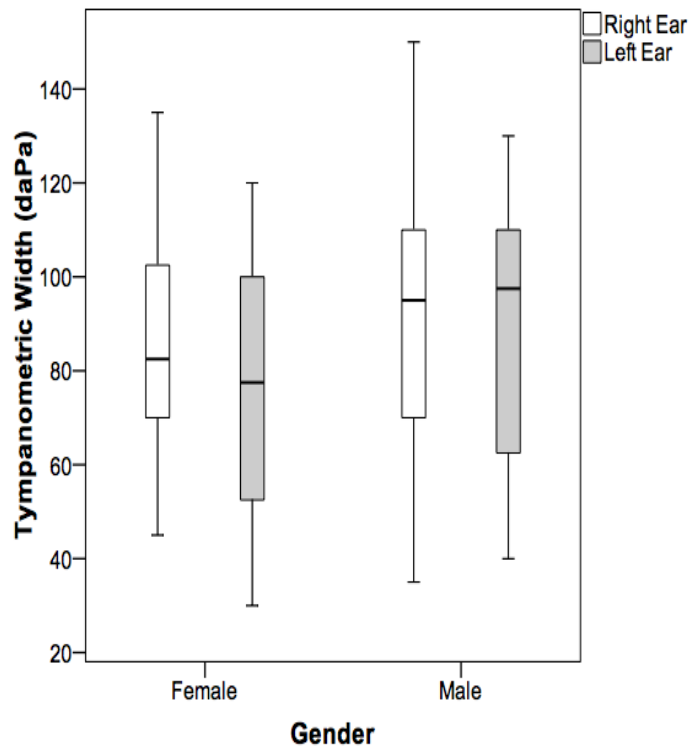
Table 26: *Mean Middle Ear Indices as a Function of Ear and Gender.*

		$Y_{tm}$	TW	TPP	$V_{ea}$
Male (N=16)					
Ear					
	Right	0.9	91	20	1.6
		(0.4)	(29)	(9)	(0.4)
	Left	0.9	90	19	1.7
		(0.5)	(28)	(5)	(0.3)
Female (N=16)					
Ear					
	Right	0.7	85	17	1.2
		(0.4)	(24)	(10)	(0.3)
	Left	0.7	77	19	1.2
		(0.3)	(29)	(8)	(0.3)

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

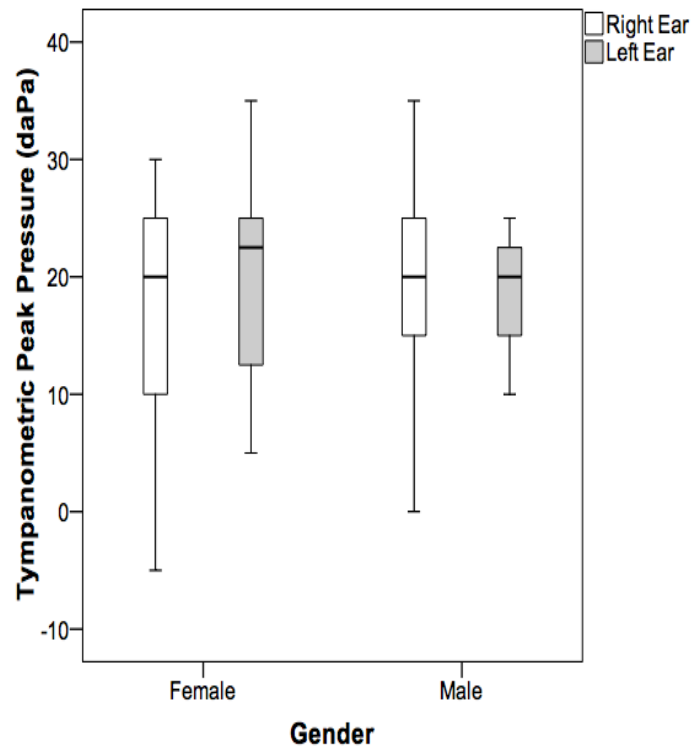


*Figure 31.* Boxplots of peak compensated static acoustic admittance (mmhos) as a function of gender and ear. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

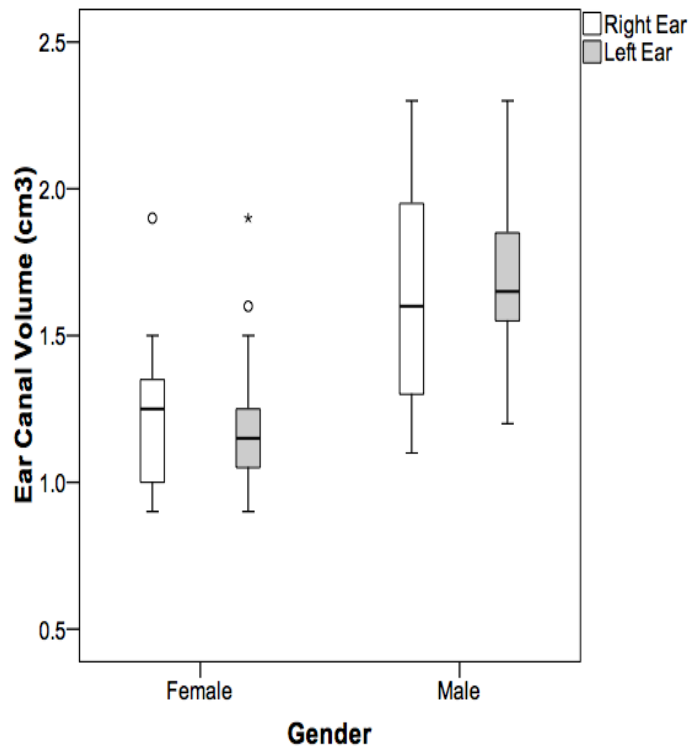


*Figure 32.* Boxplots of tympanometric width (daPa) as a function of gender and ear. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).





*Figure 33.* Boxplots of tympanometric peak pressure (daPa) as a function of gender and ear. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).



*Figure 34.* Boxplots of ear canal volume ( $\text{cm}^3$ ) as a function of gender and ear. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

Table 27. *Summary of Two-Factor Mixed Measures ANOVA Comparing Differences Between  $Y_{tm}$  (in mmho) as a Function of Ear and Gender.*

Source	Sum of Squares	<i>df</i>	Mean Square	<i>F</i>	<i>p</i>	$\eta_p^2$
Ear	0.00	1	0.00	0.01	.94	.00
Gender	0.58	1	0.58	2.08	.16	.07
Ear X Gender	0.01	1	0.01	0.44	.51	.01

*Note.* *N* = 32 for ANOVA; \*statistically significant at  $p < .05$ ; <sup>a</sup>Greenhouse-Geisser value.

Table 28. *Summary of Two-Factor Mixed Measures ANOVA Comparing Differences Between TW (in daPa) as a Function of Ear and Gender.*

Source	Sum of Squares	<i>df</i>	Mean Square	<i>F</i>	<i>p</i>	$\eta_p^2$
Ear	351.56	1	351.56	0.89	.35	.03
Gender	1501.56	1	1501.56	1.30	.26	.04
Ear X Gender	225.00	1	225.00	0.57	.46	.02

*Note.* *N* = 32 for ANOVA; \*statistically significant at  $p < .05$ ; <sup>a</sup>Greenhouse-Geisser value.

Table 29. *Summary of Two-Factor Mixed Measures ANOVA Comparing Differences Between TPP (in daPa) as a Function of Ear and Gender.*

Source	Sum of Squares	<i>df</i>	Mean Square	<i>F</i>	<i>p</i>	$\eta_p^2$
Ear	14.06	1	14.06	0.39	.55	.01
Gender	25.00	1	25.00	0.25	.62	.01
Ear X Gender	39.06	1	39.06	1.02	.32	.03

*Note.* *N* = 32 for ANOVA; \*statistically significant at  $p < .05$ ; <sup>a</sup>Greenhouse-Geisser value.

Table 30. *Summary of Two-Factor Mixed Measures ANOVA Comparing Differences Between  $V_{ea}$  (in  $\text{cm}^3$ ) as a Function of Ear and Gender.*

Source	Sum of Squares	<i>df</i>	Mean Square	<i>F</i>	<i>p</i>	$\eta_p^2$
Ear	0.01	1	0.01	0.30	.59	.01
Gender	2.93	1	2.93	20.15	<.0001*	.40
Ear X Gender	0.03	1	0.03	1.04	.32	.03

*Note.* *N* = 32 for ANOVA; \*statistically significant at  $p < .05$ ; <sup>a</sup>Greenhouse-Geisser value.

## **Apparatus**

A GSI 61™ audiometer was utilized to obtain behavioral thresholds and was the source for the 105 dBA 2000 Hz narrowband noise stimuli eliciting the noise exposure. Tympanometric measures, acoustic reflex thresholds, and acoustic reflex latency indices were obtained using a GSI TympStar™. The 2000 Hz narrowband noise acoustic reflex stimulus was routed from the GSI 61™ audiometer to the external stimulus input jack on the GSI TympStar™. A double-walled, sound treated audiometric test room (Industrial Acoustics Corporation), meeting specifications for permissible ambient noise (American National Standards Institute, 1999), served as the test environment.

## **Experimental Signal**

Four pure-tone signals (i.e., 2000, 3000, 4000, and 6000 Hz) served as the test frequencies. Acoustic reflex thresholds were elicited by a 2000 Hz pure tone stimulus as well as a 105-dBA 2000 Hz narrowband noise, which was also employed as the noise stimulus. The amplitude as a function of time waveforms for electric and acoustic 2000 Hz narrowband noise are presented in Figures 35 and 36.

Waveforms were initially generated using SpectraPRO-FFT Spectral Analysis System software (version V.3.32.17) on a Dell Latitude D630 laptop computer. For analyses of acoustic stimuli, the signals were generated by the GSI 61™ audiometer. The 2000 Hz narrowband noise was routed in series from the insert earphone to a 2cc coupler (Brüel and Kjær type DB 0138), pressure condenser microphone (Brüel and Kjær type 4144), and sound level meter (Brüel and Kjær Type 2231). The signal was then routed to a Dynamic Signal Acquisition System (model ST191DSA) signal

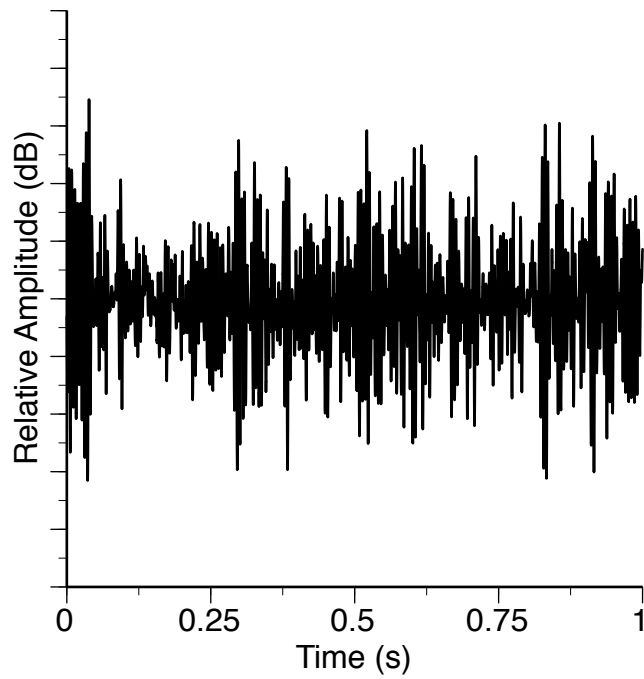
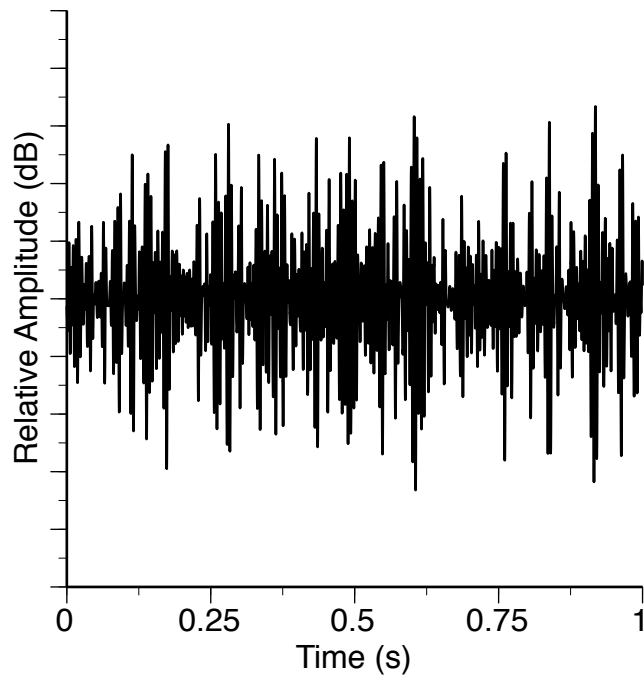


Figure 35. Amplitude as a function of time waveform of one second of an electric 2000 Hz narrowband noise.





*Figure 36.* Amplitude as a function of time waveform of one second of an acoustic 2000 Hz narrowband noise.

generator that interfaced with the Dell Latitude laptop containing the SpectraPRO software.

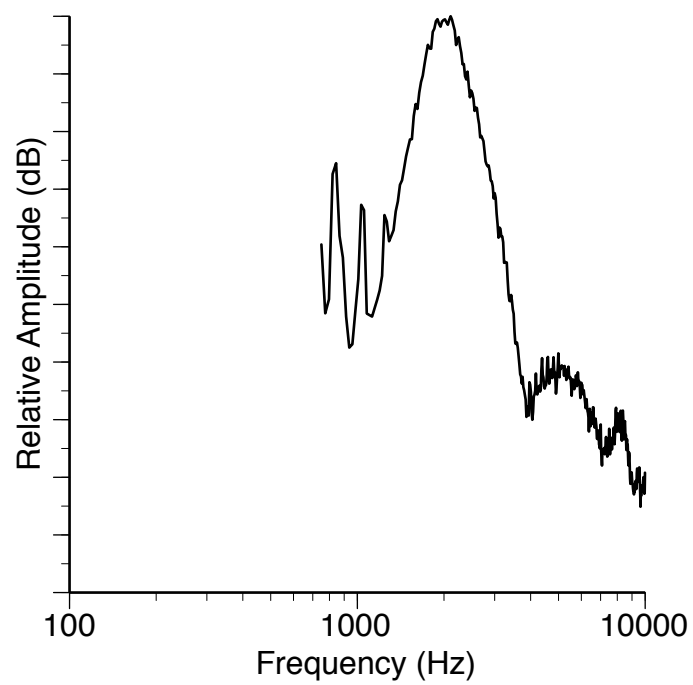
For analyses of electrical stimuli, the signal was also generated by the GSI 61™ audiometer and was transmitted directly to the Dynamic Signal Acquisition System (model ST191DSA) signal generator that interfaced with the Dell Latitude laptop containing the SpectraPRO software. Data points were copied as text files and saved using Microsoft Notepad. These points were then imported into Excel files, saved, and exported into Delta Graph. Delta Graph was used to generate graphs. SpectraPRO-FFT Signal Analysis System software was also used to perform FFTs on the electric and acoustic 2000 Hz narrowband noise (see Figures 37 and 38).

### **Stimulus Calibration**

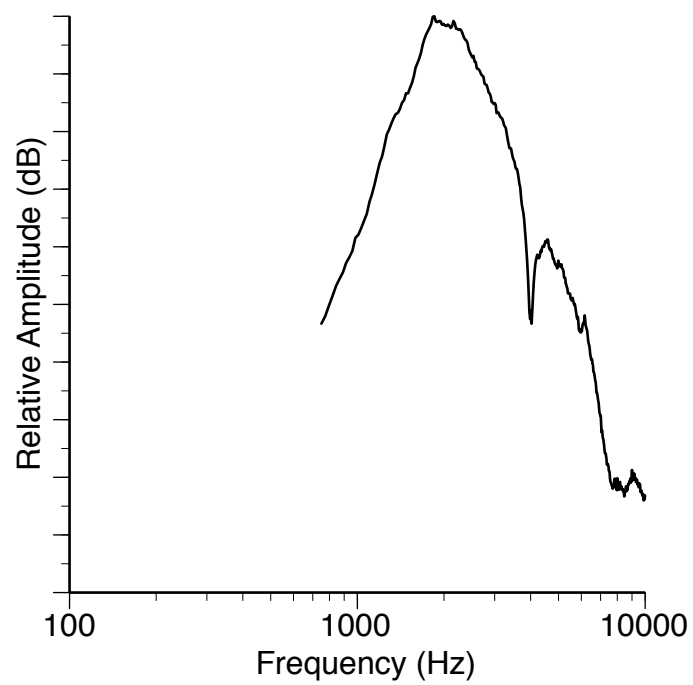
The test stimulus was calibrated to 105 dBA using a Brüel and Kjær precision sound level meter (type 2231) attached to a Brüel and Kjær pressure condenser microphone (type 4144). The 2000 Hz narrowband noise was presented using a GSI 61™ audiometer routed to an insert earphone (ER-3A) that was coupled to a Brüel and Kjær 2cc coupler (type DB 0138) attached to the sound level meter.

### **Procedure**

The University and Medical Center Institutional Review Board at East Carolina University approved this research study prior to data collection or participant recruitment (see Appendix A). Participants were recruited from the East Carolina University student body to include the School of Allied Health Sciences as well as the Department of Communication Sciences and Disorders. Participants were recruited on a volunteer basis and an informed consent was reviewed and signed by each participant prior to



*Figure 37.* FFT of an electric 2000 Hz narrowband noise.



*Figure 38.* FFT of an acoustic 2000 Hz narrowband noise.

data collection. All participants were required to meet the previously discussed inclusion criteria. During the recruiting and data collection process, funding through the East Carolina University Department of Communication Sciences and Disorders became available. Approval was obtained through the University and Medical Institutional Review Board at East Carolina University to implement this change. The allotted funds totaled \$700.00 and were distributed in \$5.00 merchandise gift cards. Thirty-two participants were paid a stipend of \$20.00 for participating in this investigation. Twelve others were paid a stipend of \$5.00 due to the fact that they did not meet inclusion criteria and were consequently removed from data collection. The participants that received compensation signed a separate informed consent prior to data collection (see Appendix C).

Behavioral thresholds, tympanometric measures, acoustic reflex indices, and noise exposure were obtained for both ears while participants were seated in a double walled sound treated audiometric suite (Industrial Acoustics Corporation) meeting the specifications for permissible ambient noise (American National Standards Institute, 1999). Intake questions were answered prior to any data collection. Otoscopy was performed to verify clear external auditory canals and visualize normal TM landmarks.

Tympanometric and acoustic reflex measures were then performed for both ears. Patients were instructed to sit quietly with limited movement throughout testing. Ipsilateral acoustic reflex thresholds for right and left ears were recorded to a 2000 Hz pure tone stimulus within the TympStar™ software and to a 2000 Hz narrowband noise routed through a GSI 61™ audiometer. Reflex threshold was identified by incrementally increasing the stimulus by 5 dB steps until a stapedius muscle contraction occurred.

Thresholds were identified as the point at which the magnitude of the deflection was at least 0.02 mmhos, was confirmed if the deflection increased in magnitude with a subsequent increase in stimulus level, and was verified by five consecutive recordings. Acoustic reflex latency measures were then obtained at 10 dB SL relative to the ipsilateral 2000 Hz pure tone acoustic reflex threshold. These values were prepopulated within the TympStar™ software. Pre-exposure behavioral thresholds were then obtained by a research assistant using the procedure recommended by ASHA (2005). The principle investigator was blind to the pre-exposure thresholds. Participants were then exposed binaurally to a 2000 Hz narrowband noise presented at 105 dBA for ten minutes. Immediately following exposure, behavioral threshold testing was completed for four frequencies: 2000 Hz, 3000 Hz, 4000 Hz, and 6000 Hz. Testing was counterbalanced by ear and frequency. A follow-up audiogram was also obtained after 48 hours to verify the return of thresholds to pre-exposure values. Mean follow-up hearing thresholds as a function of frequency, ear, and gender are shown in Table 31.

## **Results**

All descriptive and inferential analyses were conducted with IBM SPSS Statistics for Mac (Version 23.0.0.0). Signed differences in auditory thresholds were calculated by subtracting the post-noise exposure auditory threshold from the pre-noise exposure auditory threshold (Hooks-Horton et al., 2001). Positive and negative differences reflect decreases and increases, respectively in auditory thresholds.

Table 31. *Mean Follow Up Hearing Thresholds (dB HL) as a Function of Frequency, Ear, and Gender.*

		Frequency (Hz)							
		250	500	1000	2000	3000	4000	6000	8000
Male (N=10)									
Ear									
	Right	10.0	10.0	9.0	7.0	6.0	5.5	3.0	-1.5
		(4.1)	(3.3)	(3.2)	(4.8)	(5.2)	(3.7)	(5.9)	(4.7)
	Left	8.5	9.5	7.0	6.5	6.5	6.0	5.5	-2.0
		(4.7)	(2.8)	(4.8)	(4.1)	(5.8)	(4.6)	(6.0)	(6.7)
Female (N=15)									
Ear									
	Right	9.0	8.7	7.7	5.3	5.7	1.0	-0.3	-3.7
		(4.3)	(4.4)	(4.2)	(5.5)	(6.5)	(4.3)	(4.4)	(6.1)
	Left	7.0	6.7	5.0	4.7	4.0	0.3	0.3	-3.7
		(4.9)	(4.1)	(4.6)	(6.7)	(5.7)	(6.7)	(5.5)	(5.2)

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

## Auditory Threshold Differences

Means and standard deviations for auditory threshold differences as a function of frequency, ear, and gender can be found in Table 32. Boxplots (Figure 39) were also constructed to visualize data and check the assumption of normalcy. A three-factor mixed repeated measures ANOVA was conducted to examine auditory threshold differences as a function of frequency, ear, and gender. The ANOVA summary is shown in Table 33. Greenhouse-Geisser values are reported when Mauchly's Test showed that the sphericity condition was not satisfied. The main effects of frequency ( $p < .0001$ ) and ear ( $p < .0001$ ) were significant. The main effect of gender was not statistically significant. No significant two- or three- way interactions were found. Two sets of three orthogonal single- $df$  comparisons were undertaken to find the source of the main effect of frequency for the right and left ear auditory threshold differences. For the right ear, there was no significant difference between 2000 Hz and 6000 Hz ( $p = .48$ ,  $\eta_p^2 = .016$ ) and between 3000 Hz and 4000 Hz ( $p = .18$ ,  $\eta_p^2 = .056$ ). There was a significant difference between 2000 Hz and 3000 Hz and 4000 Hz ( $p < .001$ ,  $\eta_p^2 = .47$ ). In the left ear, the same was observed: There was no significant difference between 2000 Hz and 6000 Hz ( $p = .12$ ,  $\eta_p^2 = .075$ ) and between 3000 Hz and 4000 Hz ( $p = .12$ ,  $\eta_p^2 = .078$ ). There was a significant difference between 2000 Hz and 3000 Hz and 4000 Hz ( $p < .001$ ,  $\eta_p^2 = .55$ ). Larger auditory threshold differences were observed for left ears ( $M = -8.91$ ) than for right ears ( $M = -6.41$ ) and at 4000 Hz ( $M = -10.70$ ) and 3000 Hz ( $M = -9.06$ ) than for 2000 Hz ( $M = -4.77$ ) and 6000 Hz ( $M = -6.09$ ). Collapsed across gender, mean auditory threshold differences as a function of ear and frequency can be seen in Figure 40.



Table 32. *Mean Auditory Threshold Differences as a Function of Frequency, Ear, and Gender.*

		Frequency (Hz)			
		2000	3000	4000	6000
Male (N=16)					
Ear					
	Right	-3.8	-7.8	-10.0	-5.0
		(3.9)	(4.5)	(4.5)	(4.8)
	Left	-5.9	-10.0	-11.9	-7.8
		(4.2)	(3.2)	(4.4)	(5.2)
Female (N=16)					
Ear					
	Right	-3.8	-8.1	-8.8	-4.1
		(5.0)	(5.7)	(5.9)	(6.6)
	Left	-5.6	-10.3	-12.2	-7.5
		(4.4)	(6.7)	(6.0)	(7.5)

*Note.* Values enclosed in parentheses represent one standard deviation of the mean; negative values reflect an elevation in auditory threshold.

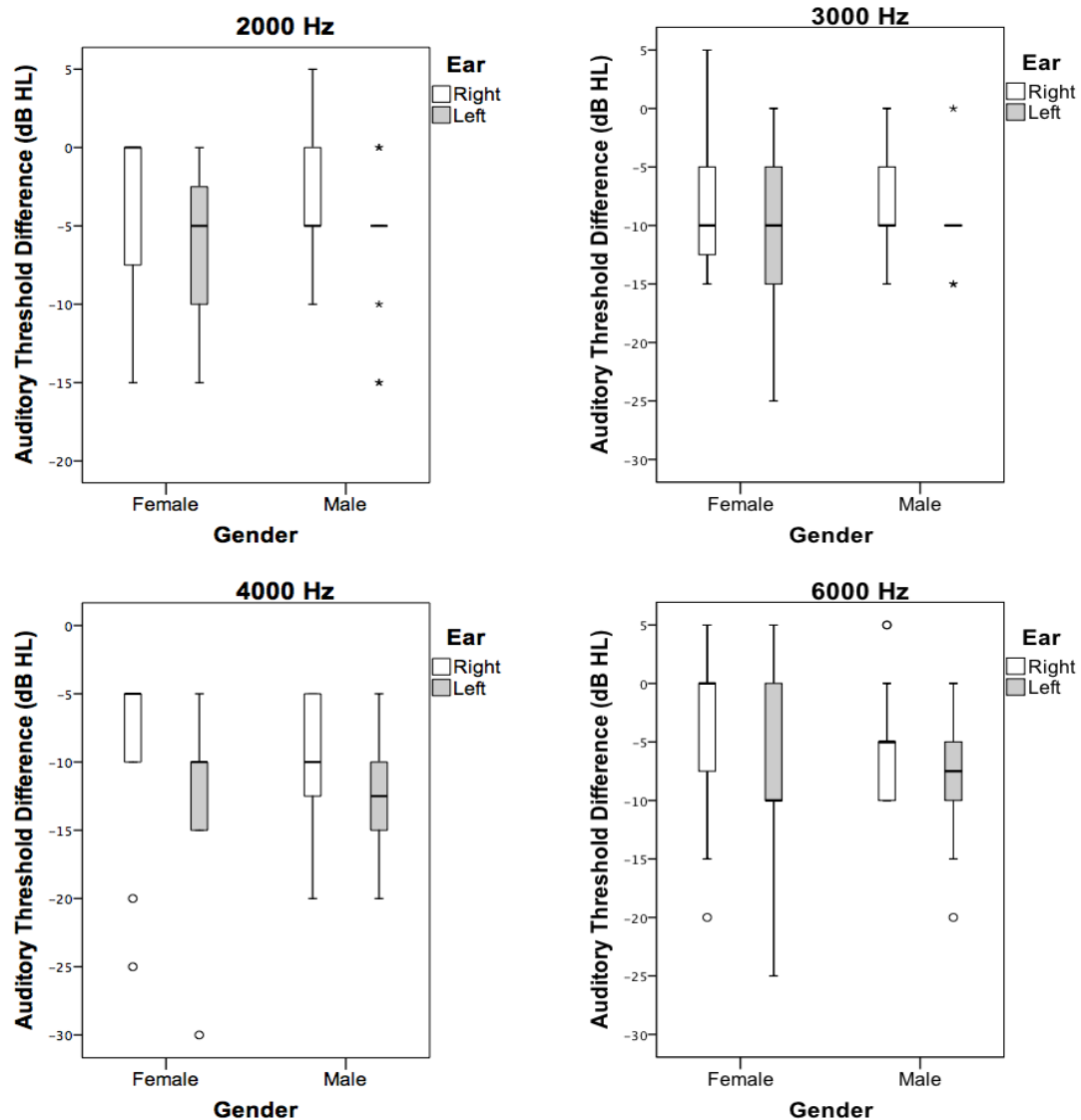
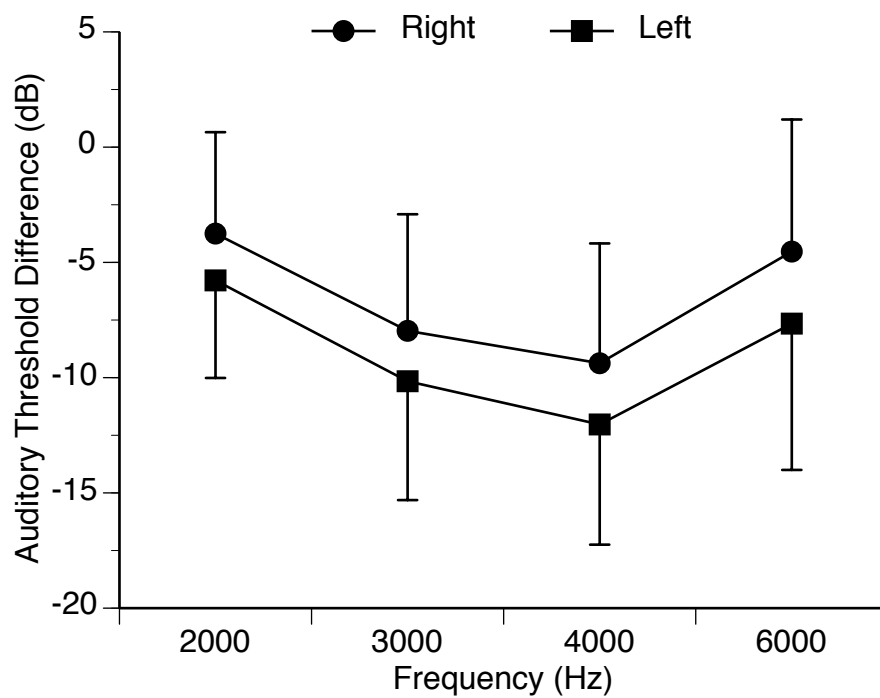


Figure 39. Boxplots of auditory threshold differences as a function of frequency, ear, and gender. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

Table 33. *Summary of Three-Factor Mixed Measures ANOVA Comparing Mean Auditory Threshold Differences as a Function of Frequency, Ear, and Gender.*

Source	Sum of Squares	<i>df</i>	Mean Square	<i>F</i>	<i>p</i>	$\eta_p^2$
Frequency	1411.72	3	470.57	15.23	<.0001*	.34
Ear	400.00	1	400.00	21.00	<.0001*	.41
Gender	3.52	1	3.52	0.04	.84	.00

*Note.* *N* = 32 for ANOVA; \*statistically significant at  $p < .05$ . A fixed factorial model was first utilized and all interactions were not statistically significant ( $p > .05$ ). The analysis was then repeated with a fixed main effects model with the same findings as reported in this table.



*Figure 40.* Mean Auditory Threshold Differences (dB) as a Function of Ear and Frequency. Error bars represent one *SD*. Negative differences reflected increases in auditory thresholds.

Pearson's product-moment correlation coefficients ( $r$ ) were initially utilized to examine the association between right and left auditory threshold differences at each of the four frequencies tested. The correlation summary is found in Table 34. There were statistically significant correlations between right ear and left ear auditory threshold differences at 3000 Hz, 4000 Hz, and 6000 Hz. To explore the relationship between auditory threshold differences at each of the four frequencies a number of bivariate scatterplots were constructed. These can be found in Figure 41.

### **Acoustic Reflex Indices**

Pearson's product-moment correlation coefficients ( $r$ ) were employed to examine the association between auditory threshold differences and ipsilateral acoustic reflex threshold to a 2000 Hz pure tone and a 2000 Hz narrowband noise. The correlation summaries are found in Tables 35 and 36. There were statistically significant correlations between right ear auditory threshold difference at 3000 Hz and right 2000 Hz pure tone acoustic reflex threshold ( $r = .38, p = .04$ ). There were also statistically significant correlations between left ear auditory threshold differences at 3000 Hz and left 2000 Hz pure tone acoustic reflex threshold ( $r = .40, p = .03$ ) and 2000 Hz narrowband noise acoustic reflex threshold ( $r = .46, p = .01$ ). To explore whether there was a relationship between auditory threshold differences and acoustic reflex threshold a number of bivariate scatterplots were constructed. These can be found in Figures 42 through 45.

In addition, Pearson's product-moment correlation coefficients ( $r$ ) were also determined to examine the association between TTS and acoustic reflex latency. Acoustic reflex latency was measured as the point at which the reflex amplitude reaches

Table 34. *Correlations Between Right Ear and Left Ear Auditory Threshold Differences as a Function of Frequency.*

	2000 Hz	3000 Hz	4000 Hz	6000 Hz
<i>r</i>	.31	.66**	.41*	.68**
<i>p</i>	.08	<.0001	.02	<.0001

*Note.* *N* = 32; \*statistically significant at the 0.05 level (2-tailed); \*\*. statistically significant at the 0.01 level (2-tailed).

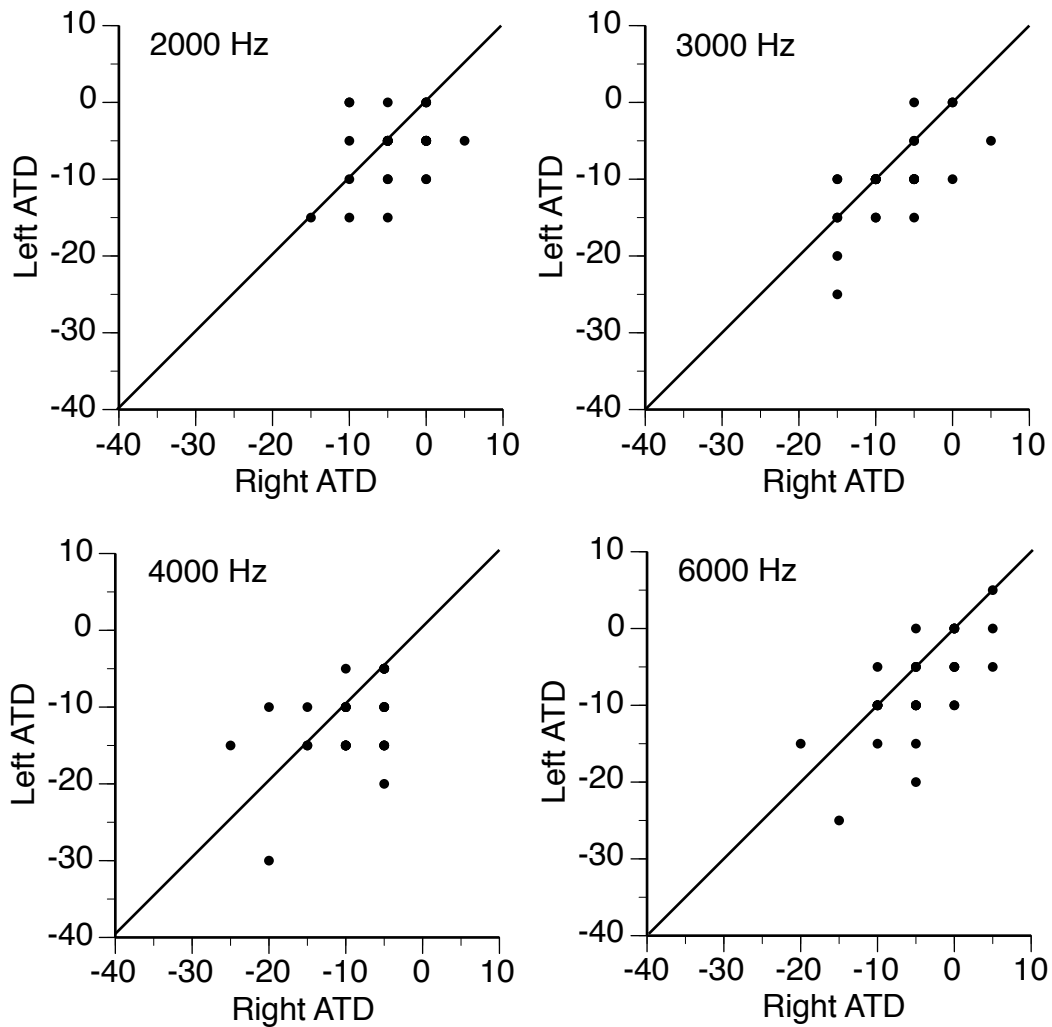


Figure 41. Bivariate scatter plots with line of equality for auditory threshold differences (dB HL) for right and left ears as a function of frequency.

Table 35. *Correlations Between Right Auditory Threshold Differences and Right Ipsilateral Acoustic Reflex Thresholds to 2000 Hz Pure Tone Stimuli and 2000 Hz Narrowband Noise Stimuli.*

Measure		Right 2000 Hz	Right 3000 Hz	Right 4000 Hz	Right 6000 Hz
Right 2000 Hz Pure Tone Acoustic Reflex Threshold	<i>r</i>	.23	.38*	-.03	.11
	<i>p</i>	.22	.04	.86	.58
	<i>N</i>	30	30	30	30
Right 2000 Hz Narrowband Noise Acoustic Reflex Threshold	<i>r</i>	.25	.26	.01	.14
	<i>p</i>	.17	.16	.95	.43
	<i>N</i>	32	32	32	32

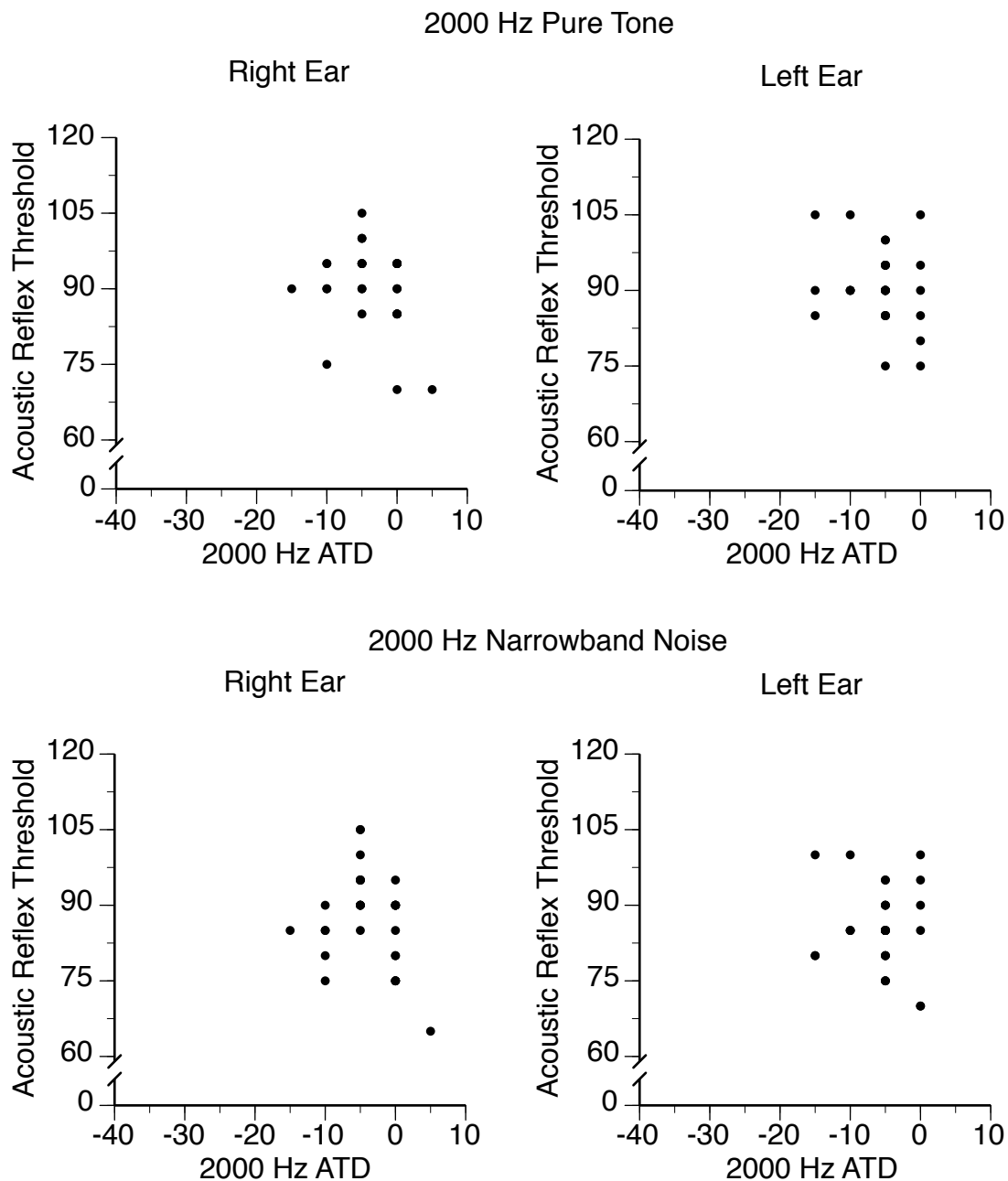
*Note.* \*statistically significant at the 0.05 level (2-tailed); \*\*. statistically significant at the 0.01 level (2-tailed).



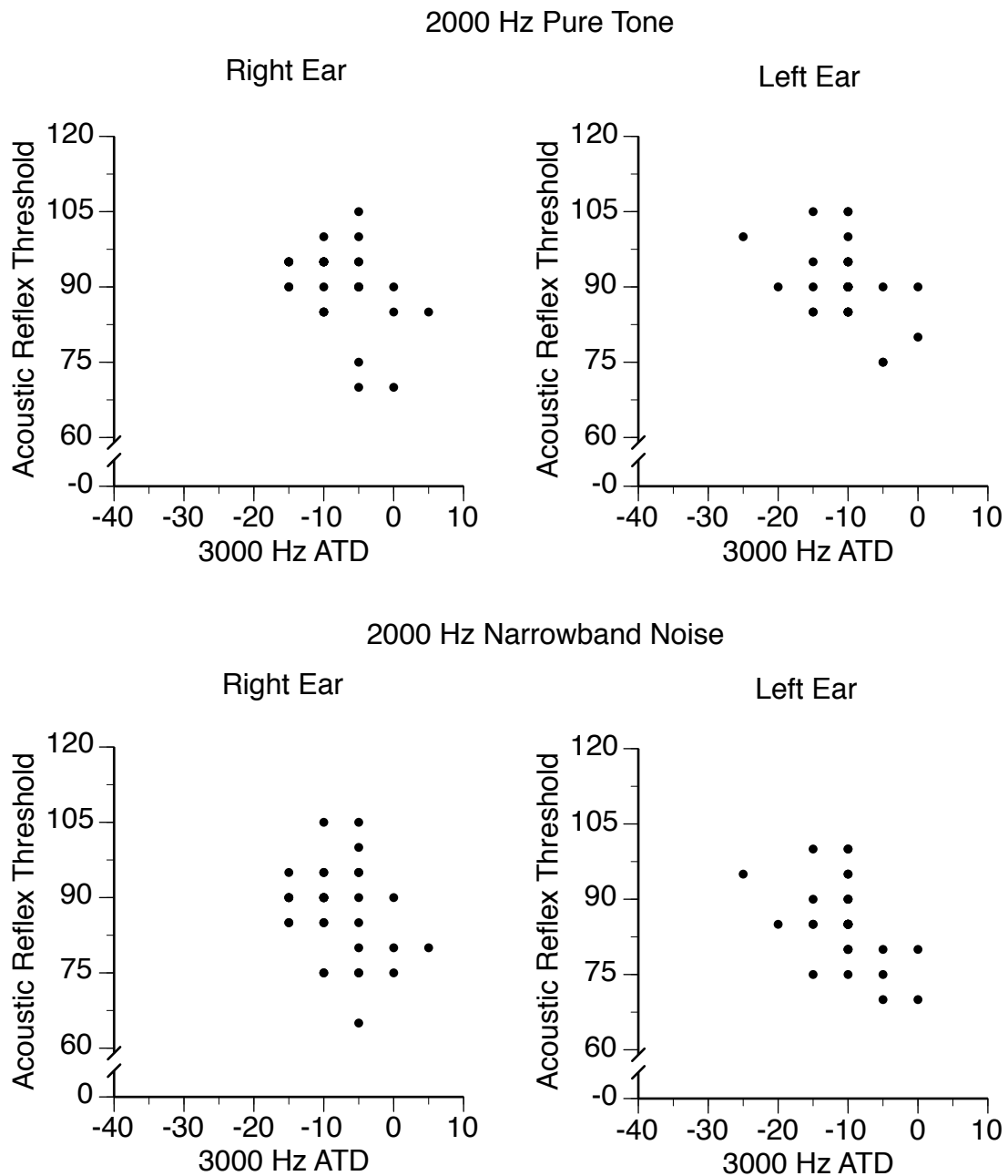
Table 36. *Correlations Between Left Auditory Threshold Differences and Left Ipsilateral Acoustic Reflex Thresholds to 2000 Hz Pure Tone Stimuli and 2000 Hz Narrowband Noise Stimuli.*

Measure		Left 2000 Hz	Left 3000 Hz	Left 4000 Hz	Left 6000 Hz
Left 2000 Hz Pure Tone Acoustic Reflex Threshold	<i>r</i>	.22	.40 <sup>*</sup>	.03	.20
	<i>p</i>	.23	.03	.88	.27
	<i>N</i>	31	31	31	31
Left 2000 Hz Narrowband Noise Acoustic Reflex Threshold	<i>r</i>	.12	.46 <sup>**</sup>	.02	.06
	<i>p</i>	.54	.01	.90	.74
	<i>N</i>	31	31	31	31

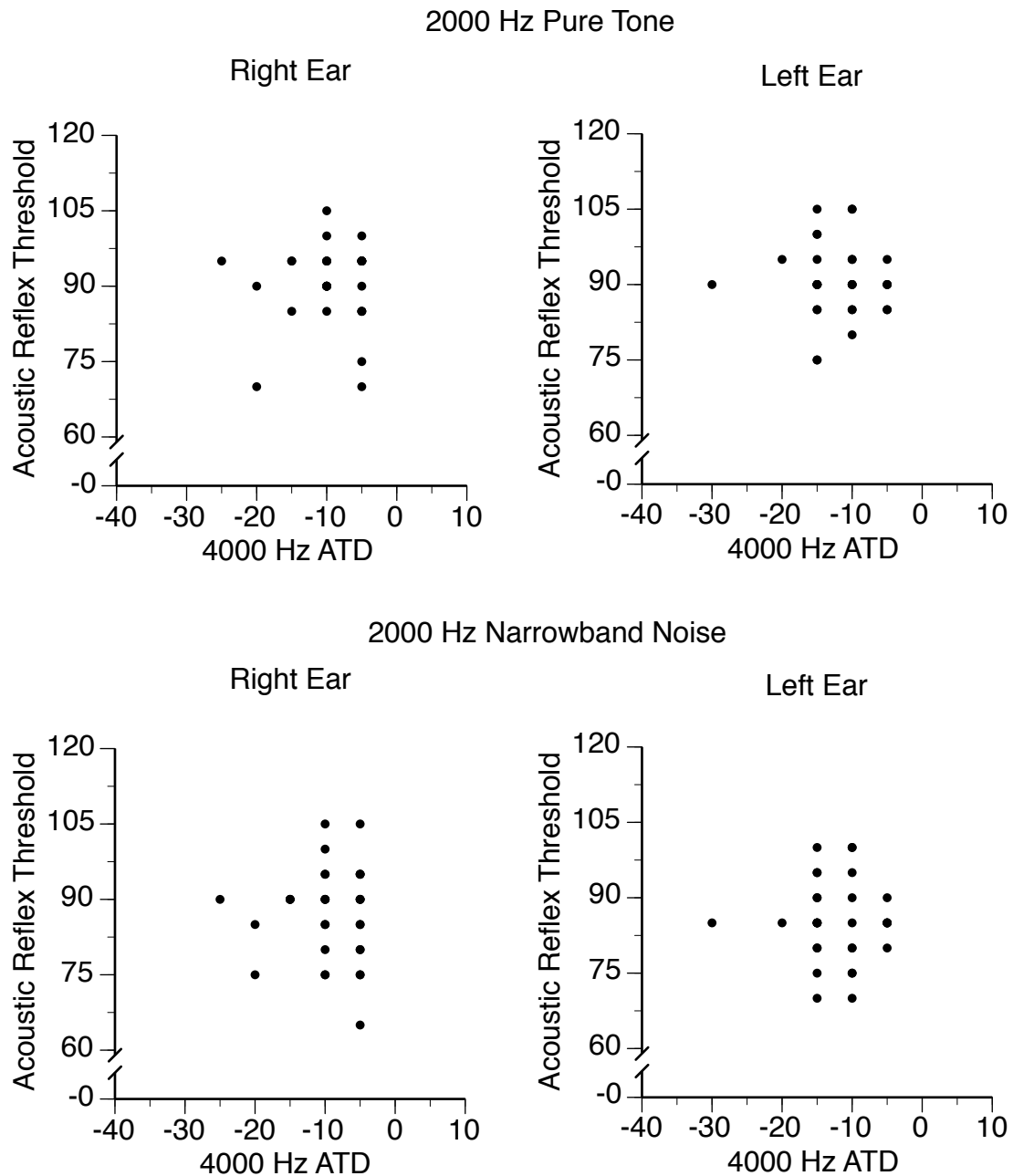
*Note.* \*statistically significant at the 0.05 level (2-tailed); \*\*. statistically significant at the 0.01 level (2-tailed).



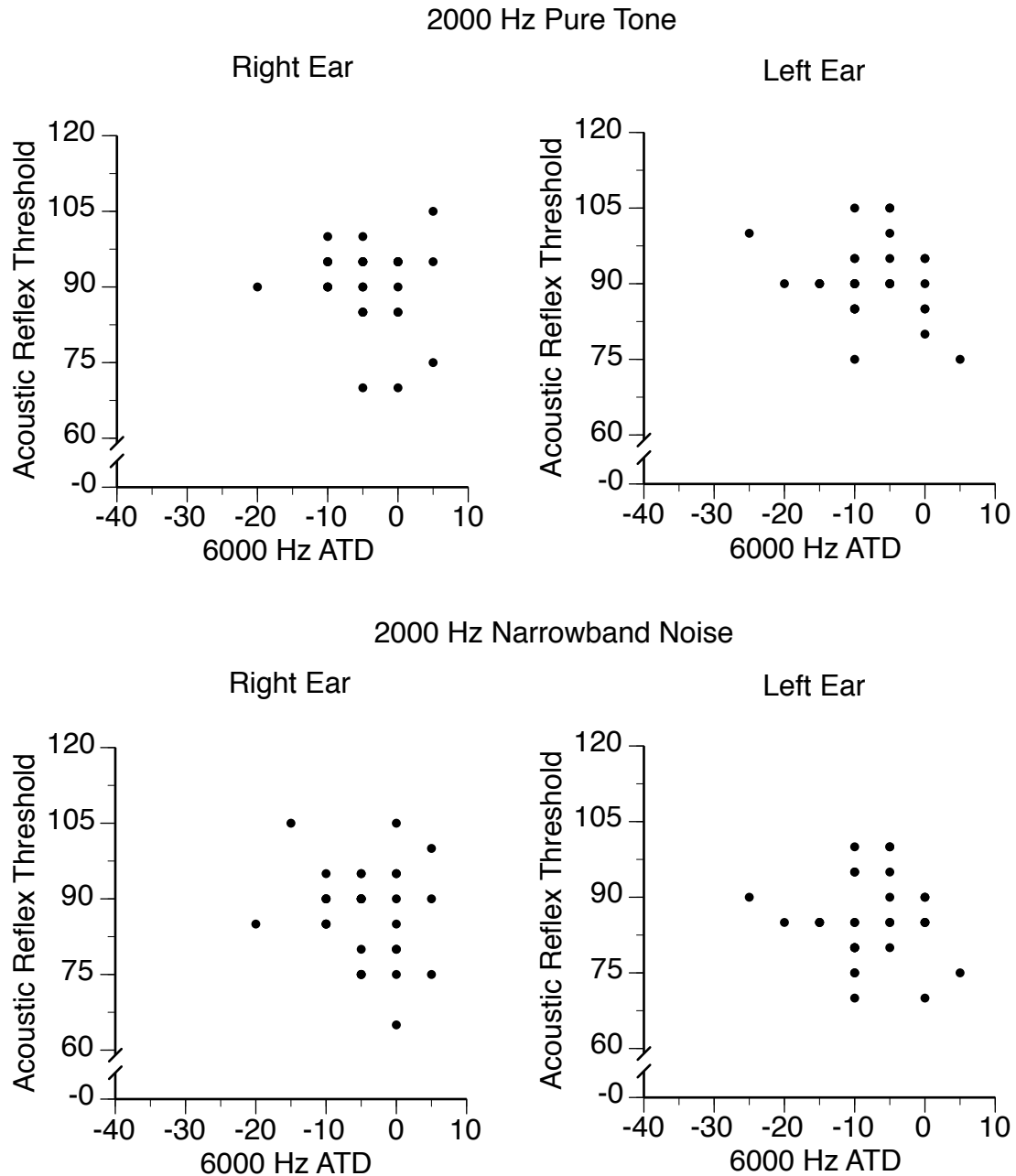
*Figure 42.* Bivariate scatter plots for 2000 Hz auditory threshold difference (dB HL) and acoustic reflex thresholds (dB SPL) to 2000 Hz pure tone and 2000 Hz narrowband noise for right and left ears.



*Figure 43.* Bivariate scatter plots for 3000 Hz auditory threshold difference (dB HL) and acoustic reflex thresholds (dB SPL) to 2000 Hz pure tone and 2000 Hz narrowband noise for right and left ears.



*Figure 44.* Bivariate scatter plots for 4000 Hz auditory threshold difference (dB HL) and acoustic reflex thresholds (dB SPL) to 2000 Hz pure tone and 2000 Hz narrowband noise for right and left ears.



*Figure 45.* Bivariate scatter plots for 6000 Hz auditory threshold difference (dB HL) and acoustic reflex thresholds (dB SPL) to 2000 Hz pure tone and 2000 Hz narrowband noise for right and left ears.

90% of its maximum amplitude (Borg, 1982; Qui & Stucker, 1998). The correlation summaries are found in Tables 37 and 38. There were no statistically significant correlations between TTS at any frequency for either ear and acoustic reflex latency ( $p > .05$ ). To explore whether there was a relationship between auditory threshold differences and acoustic reflex latency a number of bivariate scatterplots were constructed. These can be found in Figure 46.

### **Discussion**

The aim of the second experiment was to examine the effects of noise exposure on behavioral thresholds and acoustic reflex indices. Following noise exposure, a main effect of frequency was identified for behavioral thresholds. Greater auditory threshold differences were observed at approximately  $\frac{1}{2}$ -octave above the noise stimulus (i.e., 3000 Hz and 4000 Hz), which is similar to previous findings (Engdahl, 1996; Hooks-Horton et al, 2001). Additionally, a main effect of ear was identified. There were greater auditory threshold differences for left ears than for right ears. Research on gender effects for auditory threshold differences is equivocal. Similar to other research, gender differences on auditory threshold differences were identified in this study. Pirilä (1991a, b) also found that good hearing thresholds in the right ear seem to be better protected from noise-induced auditory threshold differences than good hearing thresholds in the left ear. Hooks-Horton et al. (2001) failed to find a gender effect when utilizing the same narrowband noise stimulus. Likewise, Chermak and Dengerink (1978) failed to find a gender effect when utilizing a white noise stimulus. Hori et al. (1993) found that ovarian and contraceptive cycles may play an additional role in auditory threshold differences. These factors were not controlled in the present study.

Table 37. *Correlations Between Right Auditory Threshold Differences and Right Ipsilateral Acoustic Reflex Latency.*

Measure		Right 2000	Right 3000	Right 4000	Right 6000
		Hz	Hz	Hz	Hz
Right Ipsilateral Acoustic Reflex Latency	<i>r</i>	.01	.08	-.05	-.25
	<i>p</i>	.96	.68	.80	.18
	<i>N</i>	30	30	30	30

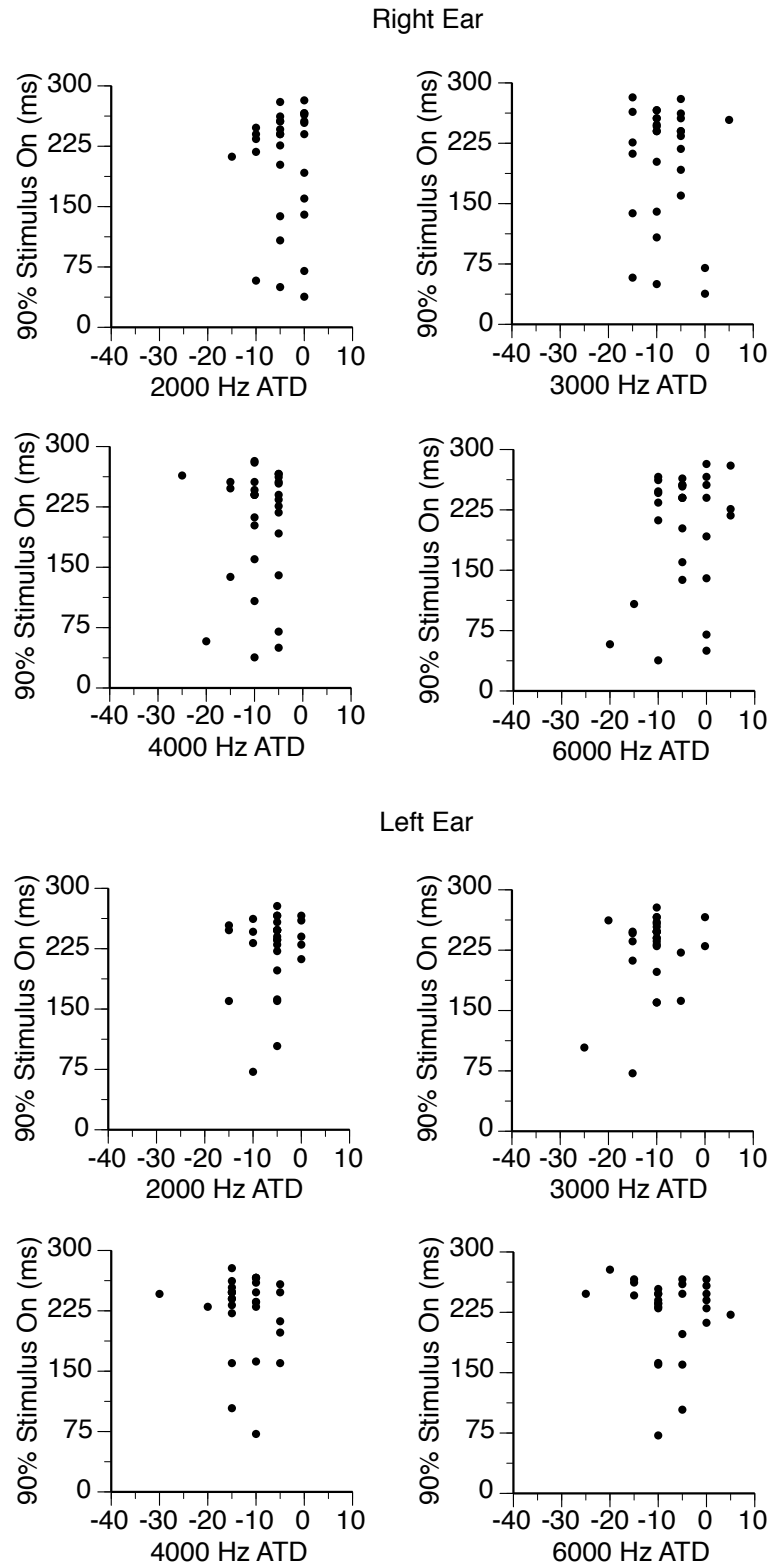
*Note.* \*statistically significant at the 0.05 level (2-tailed); \*\*. statistically significant at the 0.01 level (2-tailed).

Table 38. *Correlations Between Left Auditory Threshold Differences and Left Ipsilateral Acoustic Reflex Latency.*

Measure		Left 2000	Left 3000	Left 4000	Left 6000
		Hz	Hz	Hz	Hz
Left Ipsilateral Acoustic Reflex Latency	<i>r</i>	-.17	-.31	.12	.11
	<i>p</i>	.38	.10	.53	.59
	<i>N</i>	29	29	29	29

*Note.* \*statistically significant at the 0.05 level (2-tailed); \*\*. statistically significant at the 0.01 level (2-tailed).





*Figure 46.* Bivariate scatter plots for auditory threshold difference (dB HL) and acoustic reflex latency (ms) for both ears at each frequency.

Correlations between right auditory threshold differences and left auditory threshold differences were also examined in this study. As anticipated, right auditory threshold differences at 3000 Hz, 4000 Hz, and 6000 Hz were significantly correlated to left auditory threshold differences of the same frequencies.

The correlations between auditory threshold differences for each ear and ipsilateral acoustic reflex indices were also examined. Both right and left auditory threshold differences at 3000 Hz were significantly correlated to the ipsilateral 2000 Hz pure tone acoustic reflex threshold. In addition, left auditory threshold differences at 3000 Hz were also significantly correlated to the 2000 Hz narrowband noise ipsilateral acoustic reflex threshold. This suggests that acoustic reflex thresholds to stimuli similar as the eliciting noise stimulus could aid in the prediction of the observed auditory threshold difference. In this study it was observed that the higher the acoustic reflex threshold the greater the shift in behavioral threshold. Contrary to acoustic reflex threshold results, there were no significant correlations between auditory threshold differences and acoustic reflex latencies.

## CHAPTER IV: EXPERIMENT 3 – THE EFFECT OF NOISE EXPOSURE ON DISTORTION PRODUCT OTOACOUSTIC EMISSIONS

DPOAEs provide objective information on the integrity of outer hair cell function and have been suggested to be particularly useful for assessing damage due to noise overexposure (Marshall & Heller, 1998). They are also known to reflect the mechanical nonlinearity of the cochlea, contributing to their physiologic vulnerability to ototoxic exposure including but not limited to noise exposure (Engdahl & Kemp, 1996). The greatest sensitivity of DPOAEs to noise exposure occurs at low primary levels where DPOAE amplitude reduction is maximum (Engdahl & Kemp, 1996). DPOAE I/O functions seem to be measures of cochlear-response growth and changes in I/O functions can help describe the changes in cochlear response as a result of hearing loss in humans. Kummer et al. (1998) suggest that due to these findings DPOAEs should be measured at lower primary tone levels in addition to higher levels to aid in the prediction of the hearing threshold. Kim et al. (2005) examined DPOAE sensitivity for detecting noise-induced TTSs and found that ECoChG is a more sensitive and specific tool than DPOAEs for detecting a noise-induced TTS. Kim et al. (2005), however, did not test DPOAEs at lower primary tone levels and did not have a controlled noise source. The aim of this study was to examine the effect of noise exposure on low level evoked DPOAE absolute amplitudes in young adults.

### **Methods**

#### **Participants**

Participants were the same 32 normal hearing young adults described in Experiment 2. Briefly, they were sixteen adult males with a mean age of 25.4 ( $SD =$

2.9) years and 16 adult females with a mean age of 24.0 ( $SD = 2.4$ ) years. Participants were Caucasians with a negative history of loud noise exposure within 48 hours prior to data collection and no significant history of neurological, otological, and/or communication disorders. In examining the effect of noise exposure on DPOAEs, one ear was tested on each participant – with right and left ears counterbalanced - for a total of 32 ears. All participants had normal hearing sensitivity defined as pure tone thresholds at octave frequencies from 250 Hz to 8000 Hz  $\leq 15$  dB HL (American National Standards Institute, 2010). Participants also had normal middle ear function defined as  $Y_{tm} = 0.3$ -1.50 mmho,  $TW = 35.80$ - 95.00 daPa,  $V_{ea} = 0.9$ -1.80 cm<sup>3</sup>, and  $TPP \pm 50$  daPa (Roup et al., 1998; Marshall, Heller, & Westhusin, 1997). Mean hearing thresholds for all participants as a function of frequency, ear, and gender were displayed in Table 24 and mean tympanometric indices for all participants as a function of ear and gender were displayed in Table 26. In addition, participants were also required to have DPOAE signal to noise ratios  $\geq 6$  dB at  $f_2$  frequencies of 2051 Hz, 2783 Hz, 3760 Hz, and 4980 Hz with  $L1$  and  $L2 = 65$  dB SPL in at least one ear.

### **Apparatus and Stimuli**

A GSI 61™ audiometer was the source for the 105 dBA 2000 Hz narrowband noise stimuli eliciting the TTS. DPOAEs were recorded with a commercial DPOAE system (Otodynamics Model ILO292 Echoport USB-II) interfaced with a personal computer (Dell Inspiron 6000 Model PP12L) running Otodynamics ILO V6 Clinical OAE software. A standard transducer (Otodynamics Model UGD TE + DPOAE probe) was utilized. A double-walled, sound treated audiometric test room (Industrial Acoustics Corporation), meeting specifications for permissible ambient noise (American National

Standards Institute, 1999), served as the test environment. The 2000 Hz narrowband noise stimulus calibration was performed as described above in Chapter III.

## **Procedure**

The University and Medical Center Institutional Review Board at East Carolina University approved this research study prior to data collection or participant recruitment (see Appendix A). Participants were recruited from the East Carolina University student body to include the School of Allied Health Sciences as well as the Department of Communication Sciences and Disorders. Participants were recruited on a volunteer basis and an informed consent was reviewed and signed by each participant prior to data collection. All participants were required to meet the previously discussed inclusion criteria. During the recruiting and data collection process, funding through the East Carolina University Department of Communication Sciences and Disorders became available. Approval was obtained through the University and Medical Institutional Review Board at East Carolina University to implement this change. The allotted funds totaled \$700.00 and were distributed in \$5.00 merchandise gift cards. Thirty-two participants were paid a stipend of \$20.00 for participating in this investigation. Twelve participants were paid a stipend of \$5.00 due to the fact that they did not meet inclusion criteria and were consequently removed from data collection. The participants that received compensation signed a separate informed consent prior to data collection (see Appendix C).

Intake questions were answered prior to any data collection. Otoscopy was performed to verify clear external auditory canals and visualize normal TM landmarks. Pre-exposure behavioral thresholds were obtained by a research assistant using the

procedure recommended by ASHA (2005). The principle investigator was blind to the pre-exposure thresholds. Participants sat quietly during the collection of DPOAEs. The probe was inserted so that the proximal edge of the flange was flush with the entrance to the external auditory meatus. Pre-exposure DPOAE I/O functions were obtained at five L1, L2 levels (i.e., 65, 65 dB SPL; 60, 52.5 dB SPL; 55, 40 dB SPL; 50, 27.5 dB SPL; 45, 15 dB SPL) for four  $f_2$  frequencies (i.e., 2051 Hz, 2783 Hz, 3760 Hz, 4980 Hz). Participants were then exposed binaurally to a 2000 Hz narrowband noise presented at 105 dBA for ten minutes. Immediately following exposure, behavioral threshold testing and DPOAE testing were counterbalanced. For behavioral threshold testing, the four frequencies (i.e., 2000 Hz, 3000 Hz, 4000 Hz, 6000 Hz) were counterbalanced and thresholds were obtained using the procedure recommended by ASHA (2005). For DPOAE testing, I/O functions were obtained at five L1, L2 levels (i.e., 65, 65 dB SPL; 60, 52.5 dB SPL; 55, 40 dB SPL; 50, 27.5 dB SPL; 45, 15 dB SPL) for four  $f_2$  frequencies (i.e., 2051 Hz, 2783 Hz, 3760 Hz, 4980 Hz), which were also counterbalanced.

## **Results**

All descriptive and inferential analyses were conducted with IBM SPSS Statistics for Mac (Version 23.0.0.0). Mean and standard deviations for DPOAE absolute amplitudes at each L1, L2 level are shown in Tables 39 through 43. Only L1, L2 levels of 65, 65 dB SPL; 60, 52.5 dB SPL; and 55, 40 dB SPL were included in data analyses due to the large amount of missing data at the two lower levels. Signed differences in DPOAE amplitudes were calculated by subtracting the post-noise exposure DPOAE

Table 39. *DPOAE Mean Amplitudes and Standard Deviations as a Function of  $f_2$  Frequency, Test, Ear, and Gender at L1, L2 level of 65, 65 dB SPL.*

		f <sub>2</sub> Frequency (Hz)								
Test	Ear		Male				Female			
			2,051	2,783	3,769	4,980	2,051	2,783	3,769	4,980
Baseline										
	Right	<i>M</i>	4.9	2.5	7.0	9.5	8.6	9.1	11.0	13.6
		( <i>SD</i> )	(4.1)	(3.8)	(4.2)	(9.9)	(5.7)	(6.8)	(6.6)	(5.5)
		<i>N</i>	8	8	8	8	8	8	8	8
	Left	<i>M</i>	3.5	1.8	3.8	9.3	5.2	3.1	7.0	14.4
		( <i>SD</i> )	(4.0)	(4.8)	(5.4)	(7.8)	(6.3)	(6.7)	(3.2)	(6.6)
		<i>N</i>	8	8	8	8	8	8	8	8
Post										
Exposure										
	Right	<i>M</i>	4.1	1.4	5.2	10.3	8.6	6.8	8.0	12.8
		( <i>SD</i> )	(3.6)	(4.1)	(4.4)	(7.0)	(4.7)	(6.5)	(6.3)	(5.3)
		<i>N</i>	8	7	8	7	7	7	8	8
	Left	<i>M</i>	4.1	0.3	5.2	8.0	4.5	2.7	4.5	13.2
		( <i>SD</i> )	(4.8)	(4.2)	(5.0)	(6.1)	(5.0)	(4.6)	(5.9)	(5.1)
		<i>N</i>	8	8	8	8	8	7	8	8

*Note.* *M* = mean DPOAE absolute amplitude; *SD* = one standard deviation of the mean; *N* = sample size.

Table 40. *DPOAE Mean Amplitudes (dB SPL) and Standard Deviations as a Function of  $f_2$  Frequency, Test, Ear, and Gender at L1, L2 Level of 60, 52.5 dB SPL.*

		f <sub>2</sub> Frequency (Hz)								
Test	Ear	Male				Female				
		2,051	2,783	3,769	4,980	2,051	2,783	3,769	4,980	
Baseline										
	Right	<i>M</i>	3.2	2.0	4.6	9.2	9.2	8.2	9.3	11.2
		( <i>SD</i> )	(4.3)	(4.0)	(5.5)	(8.5)	(4.1)	(5.8)	(6.2)	(5.4)
		<i>N</i>	8	7	8	7	6	8	8	8
	Left	<i>M</i>	-0.1	-0.4	1.2	7.0	4.0	2.4	4.6	11.0
		( <i>SD</i> )	(4.5)	(4.1)	(6.6)	(5.9)	(6.0)	(5.5)	(4.2)	(6.0)
		<i>N</i>	8	7	7	7	6	6	8	8
Post										
Exposure										
	Right	<i>M</i>	3.6	0.7	1.7	5.9	4.8	3.7	4.8	9.5
		( <i>SD</i> )	(2.7)	(3.6)	(5.1)	(8.1)	(6.2)	(7.2)	(6.2)	(4.6)
		<i>N</i>	6	6	7	6	7	7	8	8
	Left	<i>M</i>	2.3	0.6	-0.1	3.7	0.8	0.4	2.1	7.8
		( <i>SD</i> )	(5.7)	(3.5)	(5.6)	(5.5)	(3.9)	(2.7)	(3.5)	(5.7)
		<i>N</i>	6	5	7	6	6	5	6	8

*Note.* *M* = mean DPOAE absolute amplitude; *SD* = one standard deviation of the mean; *N* = sample size.



Table 41. *DPOAE Mean Amplitudes (dB SPL) and Standard Deviations as a Function of  $f_2$  Frequency, Test, Ear, and Gender at L1, L2 Level of 55, 40 dB SPL.*

		f <sub>2</sub> Frequency (Hz)								
Test	Ear	Male				Female				
		2,051	2,783	3,769	4,980	2,051	2,783	3,769	4,980	
Baseline										
	Right	<i>M</i>	0.5	-0.8	2.8	10.8	3.7	5.5	4.6	8.0
		( <i>SD</i> )	(2.3)	(4.4)	(5.4)	(5.6)	(3.4)	(7.3)	(5.8)	(5.7)
		<i>N</i>	6	6	7	4	5	7	8	7
	Left	<i>M</i>	-1.1	-1.2	1.2	2.0	1.5	1.5	1.7	8.6
		( <i>SD</i> )	(5.4)	(2.4)	(5.2)	(6.6)	(3.9)	(2.4)	(2.9)	(3.0)
		<i>N</i>	4	4	4	5	3	4	7	6
Post										
Exposure										
	Right	<i>M</i>	-1.3	-1.6	1.6	2.2	1.1	4.9	0.6	4.2
		( <i>SD</i> )	(2.9)	(2.3)	(3.4)	(4.3)	(3.9)	(7.2)	(6.2)	(3.1)
		<i>N</i>	5	3	2	4	4	3	6	6
	Left	<i>M</i>	4.0	-0.3	-3.2	-0.7	-3.0	-4.6	-4.0	2.8
		( <i>SD</i> )	(4.7)	–	(2.8)	(5.9)	(1.5)	–	(2.8)	(3.2)
		<i>N</i>	2	1	2	2	3	1	2	5

*Note.* *M* = mean DPOAE absolute amplitude; *SD* = one standard deviation of the mean;

*N* = sample size.

Table 42. DPOAE Mean Amplitudes (dB SPL) and Standard Deviations as a Function of  $f_2$  Frequency, Test, Ear, and Gender at L1, L2 level of 50, 27.5 dB SPL.

		f <sub>2</sub> Frequency (Hz)								
Test	Ear	Male				Female				
		2,051	2,783	3,769	4,980	2,051	2,783	3,769	4,980	
Baseline										
	Right	<i>M</i>	-2.0	0.1	1.4	4.7	–	6.5	0.5	0.4
		( <i>SD</i> )	(1.8)	(1.5)	(2.7)	(4.7)	–	(0.1)	(4.8)	(3.1)
		<i>N</i>	2	2	3	3	0	2	5	6
	Left	<i>M</i>	-2.9	-16.7	-4.4	-7.6	-1.2	-5.9	-1.3	3.6
		( <i>SD</i> )	–	–	(2.5)	(11.8)	–	(0.8)	(5.8)	(3.0)
		<i>N</i>	1	1	2	3	1	2	2	3
Post										
Exposure										
	Right	<i>M</i>	–	-7.6	–	–	-4.6	-2.7	2.4	–
		( <i>SD</i> )	–	–	–	–	(0.3)	–	–	–
		<i>N</i>	0	1	0	0	2	1	1	0
	Left	<i>M</i>	0.9	–	–	–	–	–	–	–
		( <i>SD</i> )	–	–	–	–	–	–	–	–
		<i>N</i>	1	0	0	0	0	0	0	0

Note. *M* = mean DPOAE absolute amplitude; *SD* = one standard deviation of the mean;

*N* = sample size.

Table 43. *DPOAE Mean Amplitudes (dB SPL) and Standard Deviations as a Function of  $f_2$  Frequency, Test, Ear, and Gender at L1, L2 Level of 45, 15 dB SPL.*

			$f_2$ Frequency (Hz)							
			Male				Female			
Test	Ear		2,051	2,783	3,769	4,980	2,051	2,783	3,769	4,980
Baseline										
	Right	<i>M</i>	–	–	–	–	–	-6.0	-6.9	–
		( <i>SD</i> )	–	–	–	–	–	(1.1)	(3.5)	–
		<i>N</i>	0	0	0	0	0	2	2	0
	Left	<i>M</i>	–	–	–	–	–	–	–	-3.2
		( <i>SD</i> )	–	–	–	–	–	–	–	–
		<i>N</i>	0	0	0	0	0	0	0	1
Post										
Exposure										
	Right	<i>M</i>	–	–	–	–	–	–	–	–
		( <i>SD</i> )	–	–	–	–	–	–	–	–
		<i>N</i>	0	0	0	0	0	0	0	0
	Left	<i>M</i>	–	–	–	–	–	–	–	–
		( <i>SD</i> )	–	–	–	–	–	–	–	–
		<i>N</i>	0	0	0	0	0	0	0	0

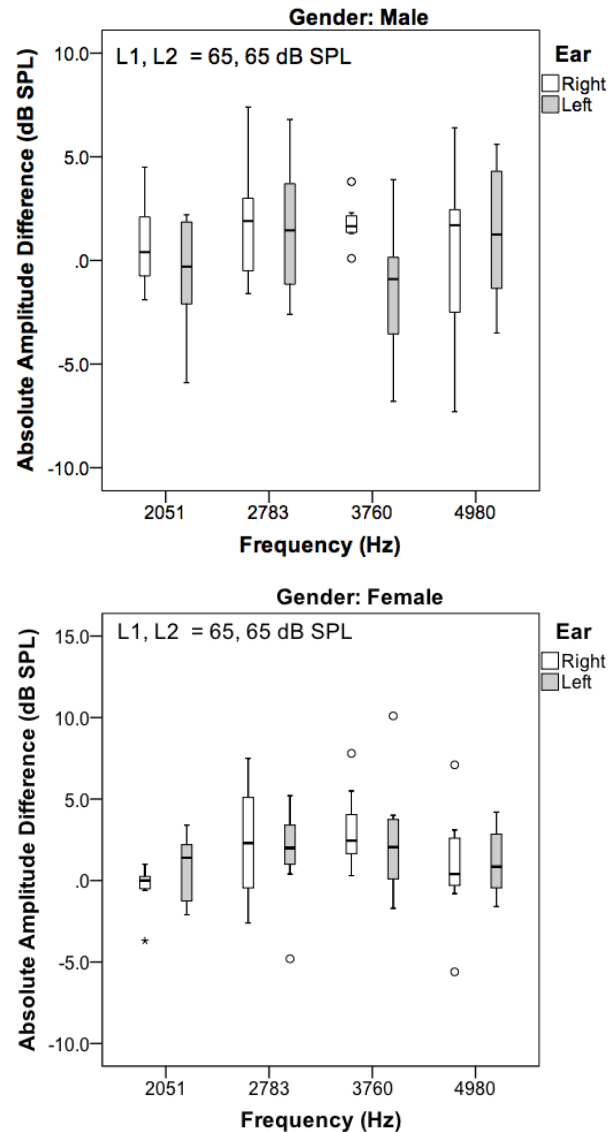
*Note.* *M* = mean DPOAE absolute amplitude; *SD* = one standard deviation of the mean;

*N* = sample size.

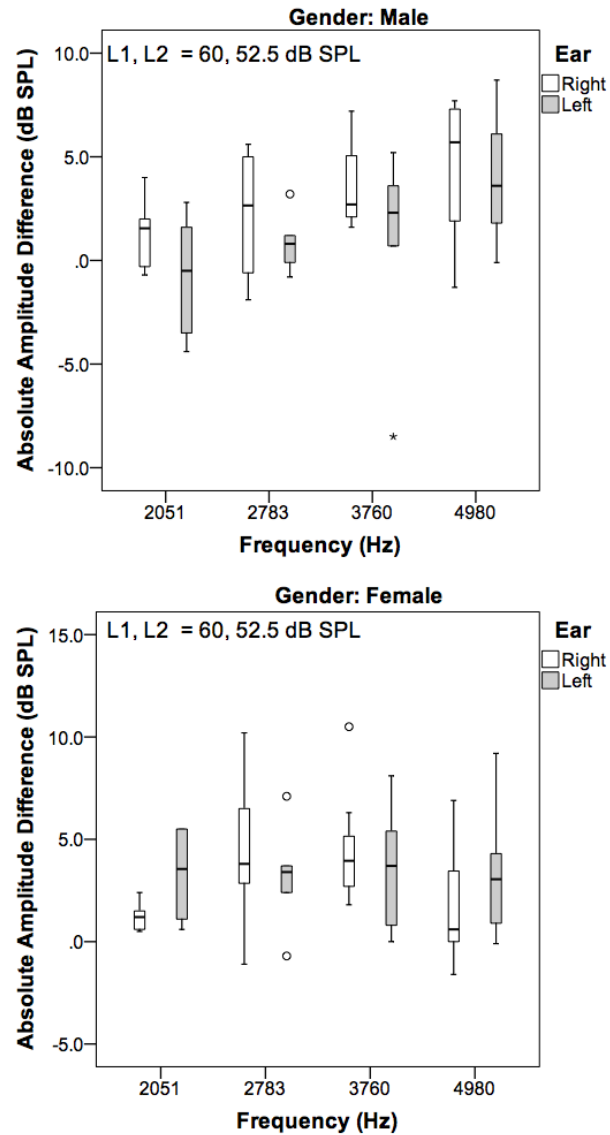
amplitude from the pre-noise exposure DPOAE amplitude (Hooks-Horton et al., 2001). Positive and negative differences reflect decreases and increases, respectively in DPOAE amplitudes. Boxplots of DPOAE absolute amplitude differences for the three highest evoking L1, L2 levels (Figures 47 to 49) were also constructed to visualize data and check the assumption of normalcy. Figures 50 through 52 display DPOAE absolute amplitudes as a function of gender, ear, test, and frequency for the three higher levels.

A four-factor factorial linear mixed model ANOVA was conducted to examine DPOAE absolute amplitude differences as a function of gender, ear, level, and frequency. The measures were modeled with a diagonal covariance metric. The choice of the covariance structure was based on goodness of fit statistics (i.e., -2 Res Log Likelihood, Akaike's information criterion, Hurvich and Tsai's Criterion, Bozdogan's Criterion, and Schwarz's Bayesian Criterion). Statistically significant main effects of level and frequency plus a single two-way interaction of gender and frequency were found ( $p < .05$ ). No other significant two-, three-, or four-way interactions were found ( $p > .05$ ). The analysis was simplified by examining the four-factor linear mixed model ANOVA with a main effects model and a two-way interaction model. The ANOVA summaries are presented in Table 44. The main effects of gender ( $p = .02$ ), level ( $p < .0001$ ), and frequency ( $p < .0001$ ) were significant. The gender by frequency and gender by ear interactions were also significant ( $p = .01$ ).

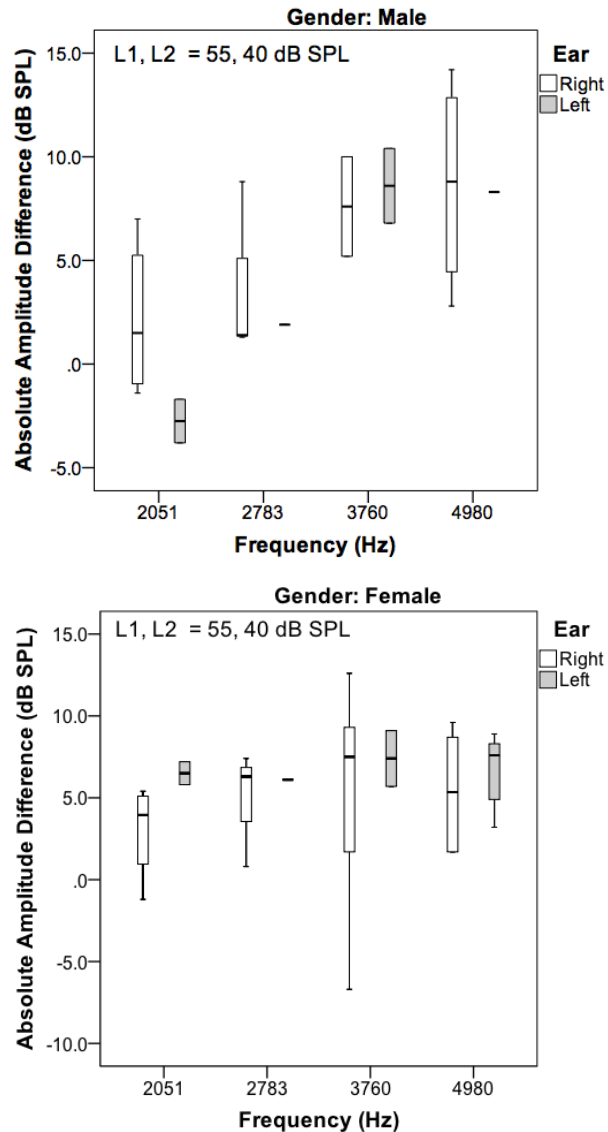
Estimated marginal mean DPOAE absolute amplitude differences as a function of level are shown in Table 45. Pairwise comparisons of DPOAE absolute amplitude differences at each L1, L2 level are displayed in Table 46. DPOAE absolute amplitude



*Figure 47.* Boxplots of DPOAE absolute amplitude differences at L1, L2 level of 65, 65 dB SPL as a function of gender, ear, and frequency. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).



*Figure 48.* Boxplots of DPOAE absolute amplitude differences at L1, L2 level of 60, 52.5 dB SPL as a function of gender, ear, and frequency. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).



*Figure 49.* Boxplots of DPOAE absolute amplitude differences at L1, L2 level of 55, 40 dB SPL as a function of gender, ear, and frequency. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

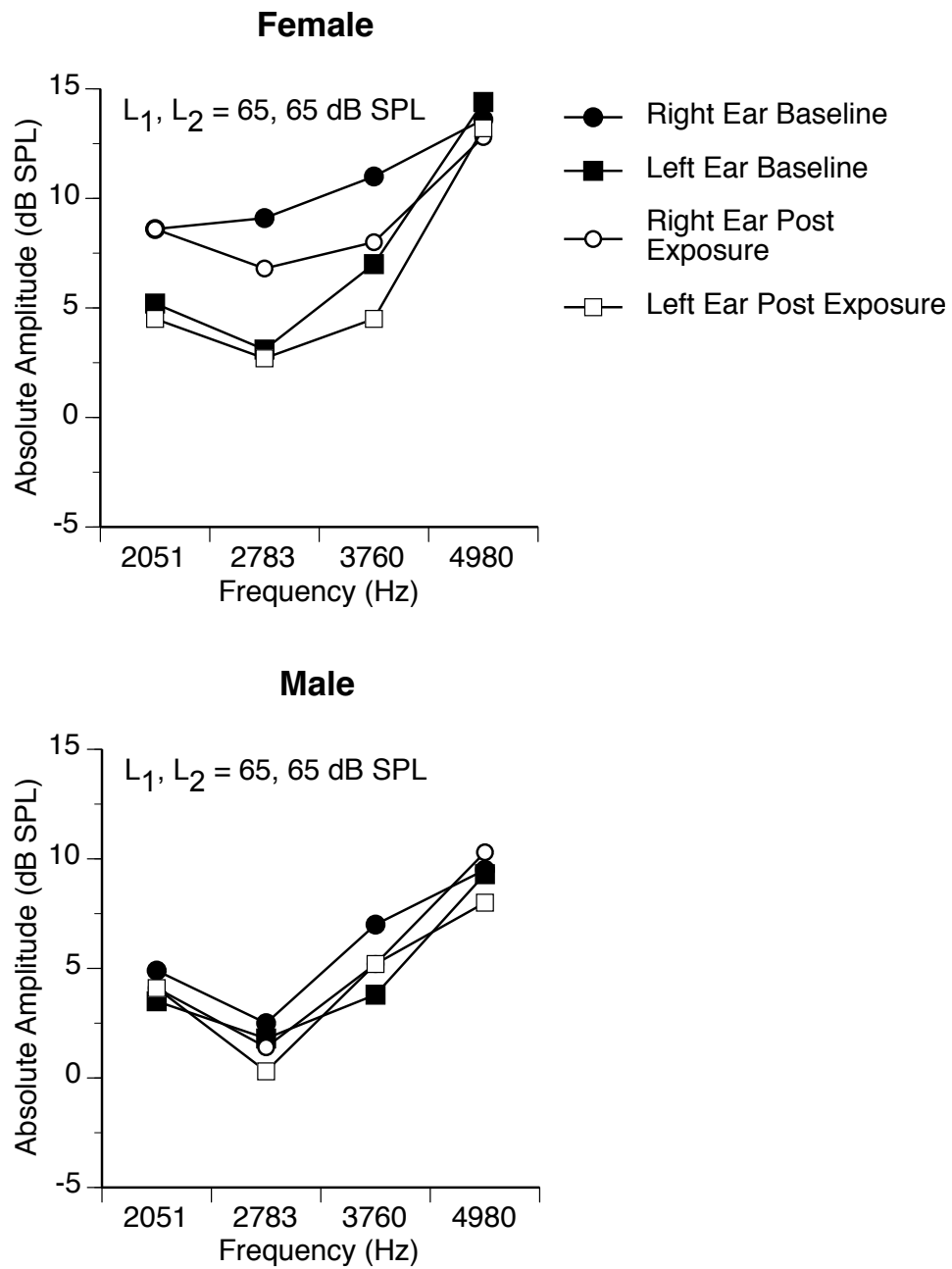


Figure 50. DPOAE absolute amplitudes (dB SPL) at  $L_1, L_2$  level of 65, 65 dB SPL as a function of gender, test, ear, and frequency.



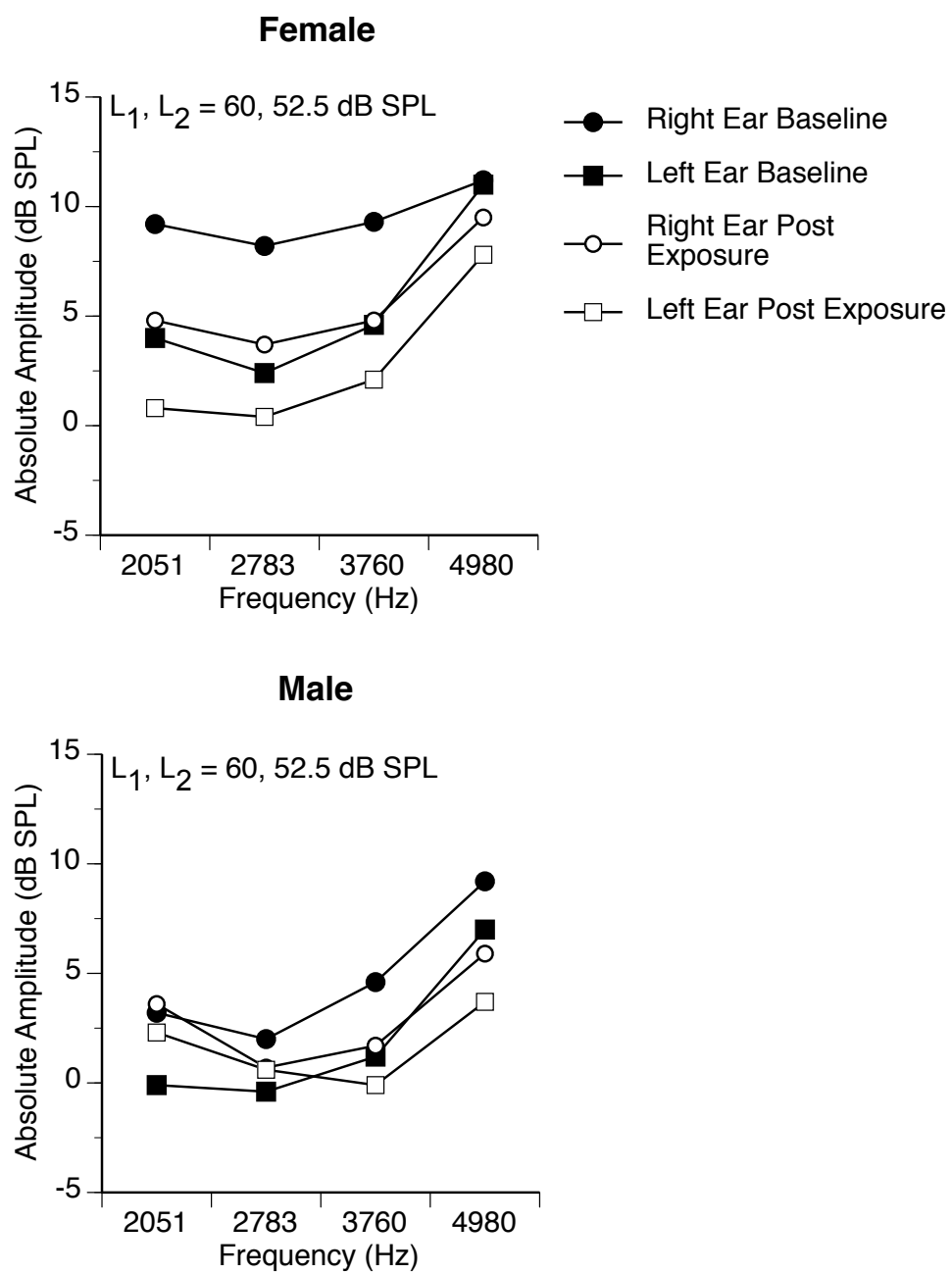


Figure 51. DPOAE absolute amplitudes (dB SPL) at  $L_1, L_2$  level of 60, 52.5 dB SPL as a function of gender, test, ear, and frequency.

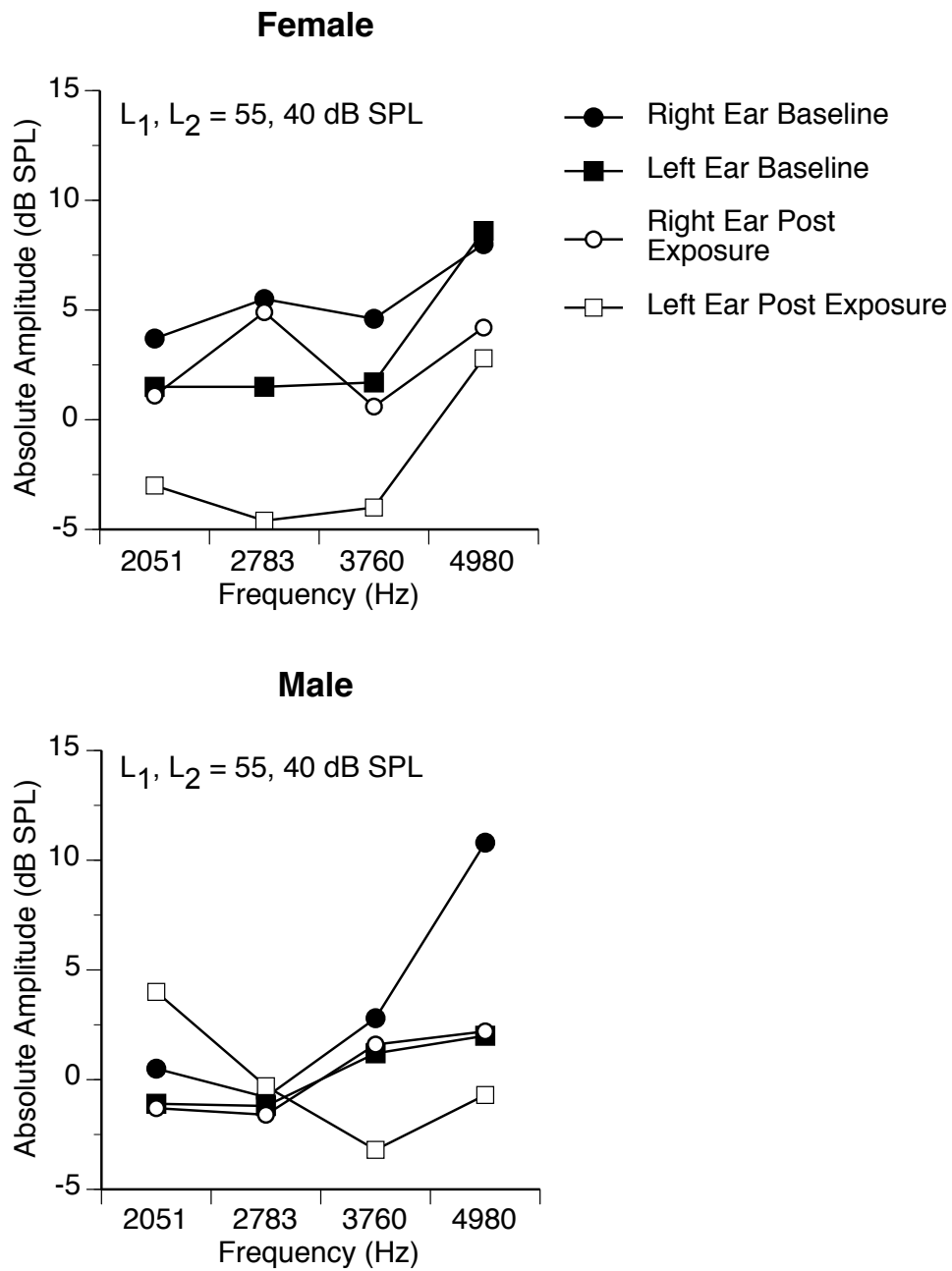


Figure 52. DPOAE absolute amplitudes (in dB SPL) at  $L_1, L_2$  level of 55, 40 dB SPL as a function of gender, test, ear, and frequency.

Table 44. *Summary of Four-Factor Linear Mixed Model ANOVA Comparing DPOAE Absolute Amplitude Differences (dB SPL) as a Function of Gender, Ear, L1, L2 Level (i.e., 65, 65 dB SPL; 60, 52.5 dB SPL; 55, 40 dB SPL), and  $f_2$  Frequency (i.e., 2051 Hz, 2783 Hz, 3760 Hz, 4980 Hz).*

Source	Numerator <i>df</i>	Denominator <i>df</i>	<i>F</i>	<i>p</i>
Gender	1	225.43	5.70	.02*
Ear	1	226.77	1.39	.24
Level	2	104.76	19.16	<.0001*
Frequency	3	119.59	6.92	<.0001*
Gender X Ear	1	208.45	6.44	.01*
Gender X Level	2	94.55	0.30	.74
Gender X Frequency	3	113.71	3.80	.01*
Ear X Level	2	95.25	0.14	.87
Ear X Frequency	3	113.76	2.04	.11
Level X Frequency	6	53.70	1.12	.36

*Note.* *N* = 32 for ANOVA; \*statistically significant at  $p < .05$ . A fixed factorial model was first utilized and only one two-way interaction was statistically significant ( $p > .05$ ). The analysis was then repeated with a fixed main effects model and then with all two-way interactions as reported in this table.

Table 45. *Estimated Marginal Mean DPOAE Absolute Amplitude Differences as a Function of Level.*

L1/L2 Level	Mean	SE	df	95% Confidence Interval	
				Lower Bound	Upper Bound
55/40	4.84	0.57	42.40	3.70	5.93
60/52.5	2.54	0.29	94.41	1.96	3.12
65/65	1.18	0.26	124.08	0.68	1.70

*Note.* Based on a fixed main effects model.

Table 46. *Pairwise Comparisons of DPOAE Absolute Amplitude Differences at Each L1, L2 Level.*

L1/L2 Level	L1/L2 Level	Mean Difference	SE	df	p	95% Confidence Interval for Difference <sup>a</sup>	
						Lower Bound	Upper Bound
55/40	60/52.5	2.30*	0.64	64.51	.001	1.02	3.58
	65/65	3.66*	0.62	60.90	<.001	2.41	4.91
60/52.5	55/40	-2.30*	0.64	64.51	.001	-3.58	-1.02
	65/65	1.35*	0.38	178.68	.001	0.59	2.11
65/65	55/40	-3.66*	0.62	60.90	<.001	-4.91	-2.41
	60/52.5	-1.35*	0.38	178.68	.001	-2.11	-0.59

*Note.* Based on estimated marginal means, \*the mean difference is significant at the .05 level, <sup>a</sup>adjustment for multiple comparisons: least significant difference (equivalent to no adjustments).

differences were statistically different for each level ( $p < .05$ ). DPOAE absolute amplitude differences were largest for the L1, L2 level of 55, 40 dB SPL and smallest for the L1, L2 level of 65, 65 dB SPL.

Estimated marginal mean DPOAE absolute amplitude differences as a function of  $f_2$  frequency are shown in Table 47. Pairwise comparisons of DPOAE absolute amplitude differences at each  $f_2$  frequency are displayed in Table 48. DPOAE absolute amplitude differences for 2051 Hz were statistically different from the other three  $f_2$  frequencies ( $p < .05$ ). DPOAE absolute amplitude differences were smallest for the  $f_2$  frequency of 2051 Hz.

Estimated marginal mean DPOAE absolute amplitude differences as a function of gender and  $f_2$  frequency are shown in Table 49. The significant gender by frequency interaction ( $p < .05$ ) is displayed in Figure 53. The data were collapsed across ear and level. Females generally had larger DPOAE absolute amplitude differences than males except at the  $f_2$  frequency of 4980 Hz.

Estimated marginal mean DPOAE absolute amplitude differences as a function of gender and ear are shown in Table 50. The significant gender by ear interaction ( $p < .05$ ) is displayed in Figure 54. The data were collapsed across frequency and level. Females had significantly larger DPOAE differences in the left ear versus males,  $t(130) = 2.71$ ,  $p = .01$ . Males had significantly larger DPOAE differences in the right ear versus the left ear,  $t(47) = 2.37$ ,  $p = .02$ .

Table 47. *Estimated Marginal Mean DPOAE Absolute Amplitude Differences as a Function of  $f_2$  Frequency.*

$f_2$ Frequency	Mean	SE	df	95% Confidence Interval	
				Lower Bound	Upper Bound
2051 Hz	1.58	0.34	76.90	0.90	2.25
2783 Hz	3.16	0.42	58.24	2.32	3.99
3760 Hz	3.41	0.42	85.26	2.57	4.24
4980 Hz	3.29	0.40	73.16	2.49	4.08

*Note.* Based on a fixed main effects model.

Table 48. *Pairwise Comparisons of DPOAE Absolute Amplitude Differences at Each  $f_2$  Frequency.*

						95% Confidence Interval for Difference <sup>a</sup>	
$f_2$	$f_2$	Mean				Lower	Upper
Frequency	Frequency	Difference	SE	df	p	Bound	Bound
2051 Hz	2783 Hz	-1.58*	0.50	107.48	.002	-2.58	-0.59
	3760 Hz	-1.83*	0.49	114.05	<.001	-2.81	-0.86
	4980 Hz	-1.71*	0.49	119.46	.001	-2.68	-0.74
2783 Hz	2051 Hz	1.58*	0.50	107.48	.002	0.59	2.58
	3760 Hz	-0.25	0.56	119.27	.66	-1.35	0.85
	4980 Hz	-0.13	0.55	125.72	.82	-1.22	0.96
3760 Hz	2051 Hz	1.83*	0.49	114.05	<.001	0.86	2.81
	2783 Hz	0.25	0.56	119.27	.66	-0.85	1.35
	4980 Hz	0.12	0.54	132.51	.82	-0.96	1.20
4980 Hz	2051 Hz	1.71*	0.49	119.46	.001	0.74	2.679
	2783 Hz	0.13	.55	125.724	.82	-0.96	1.223
	3760 Hz	-0.12	.54	132.510	.82	-1.20	0.958

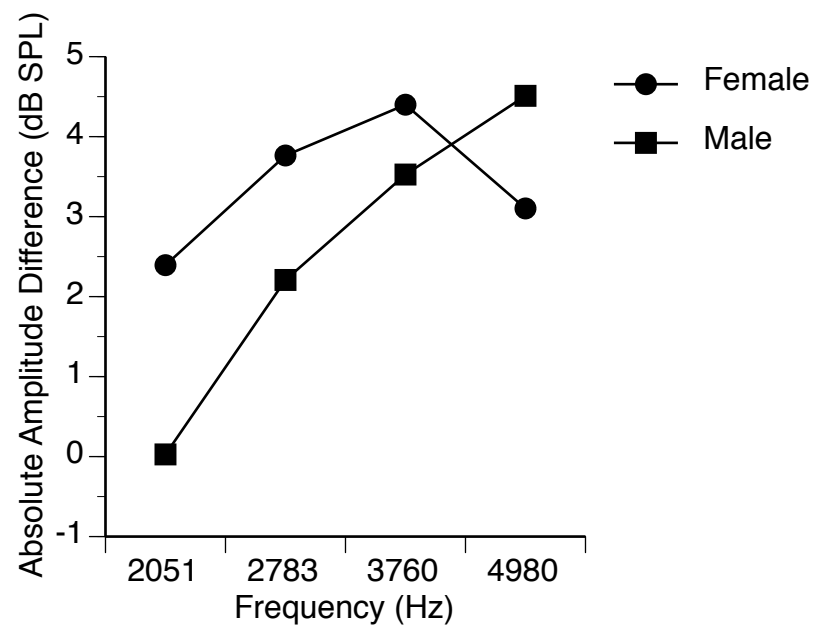
*Note.* Based on estimated marginal means, \*the mean difference is significant at the .05 level, <sup>a</sup>adjustment for multiple comparisons: least significant difference (equivalent to no adjustments).



Table 49. *Estimated Marginal Mean DPOAE Absolute Amplitude Differences as a Function of Gender and  $f_2$  Frequency.*

$f_2$		95% Confidence Interval				
Gender	Frequency	Mean	SE	df	Lower Bound	Upper Bound
Female	2051 Hz	1.81	0.53	29.43	0.72	2.90
	2783 Hz	3.68	0.65	28.86	2.35	5.00
	3760 Hz	4.71	0.69	25.77	3.30	6.12
	4980 Hz	3.16	0.49	51.39	2.17	4.15
Male	2051 Hz	0.70	0.51	27.17	-0.36	1.75
	2783 Hz	2.18	0.65	28.85	0.86	3.501
	3760 Hz	2.58	0.76	32.93	1.04	4.13
	4980 Hz	4.39	0.61	56.19	3.16	5.62

*Note.* Based on an all two-way fixed effects model.



*Figure 53.* DPOAE absolute amplitude differences (in dB SPL) collapsed across ear and level as a function of gender and frequency.

Table 50. *Estimated Marginal Mean DPOAE Absolute Amplitude Differences as a Function of Gender and Ear.*

Gender	Ear	Mean	SE	df	95% Confidence Interval	
					Lower Bound	Upper Bound
Female	Right	3.12	0.41	107.29	2.30	3.91
	Left	3.57	0.43	106.70	2.71	4.42
Male	Right	3.13	0.44	99.37	2.25	4.01
	Left	1.80	0.47	99.82	0.86	2.74

*Note.* Based on an all two-way fixed effects model.

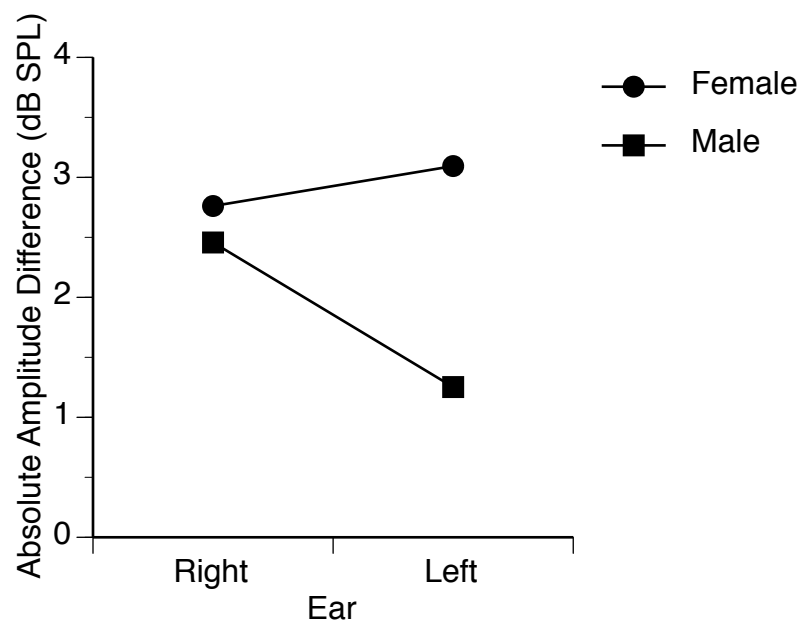


Figure 54. DPOAE absolute amplitude differences (in dB SPL) collapsed across frequency and level as a function of gender and ear.

## Discussion

The aim of the third experiment was to examine the effect of noise exposure on low level evoked DPOAE absolute amplitudes in young adults. The overall hypotheses were that DPOAE absolute amplitudes would be decreased following noise exposure and there would be a significant main effect of frequency. It was also hypothesized that there would be no main effect of gender.

In Experiment 3, DPOAE absolute amplitudes were generally decreased following noise exposure as identified by very few negative absolute amplitude differences. As predicted, baseline amplitudes were significantly larger than those following noise exposure. There was also a larger difference for the lowest L1, L2 level of 55, 40 dB SPL ( $M = 5.15$ ) than for L1, L2 = 60, 52.5 dB SPL ( $M = 2.61$ ) and L1, L2 = 65, 65 dB SPL ( $M = 1.15$ ). These findings are similar to those of Engdahl and Kemp (1996) in that they also found the degree of amplitude reduction to be greatest at low levels. Additionally, there was a statistically significant main effect of frequency. The only frequency to statistically differ from the other three was 2051 Hz. This lowest frequency had the smallest difference ( $M = 1.21$ ) while 2783 Hz ( $M = 2.90$ ), 3760 Hz ( $M = 3.96$ ), and 4980 Hz ( $M = 3.81$ ) had larger differences. These findings are also similar to previous studies utilizing the same 2000 Hz narrowband noise as the eliciting noise stimuli (Engdahl & Kemp, 1996; Hooks-Horton et al., 2001). Moreover, as observed in Experiment 2, the 2000 Hz narrowband noise exposure resulted in the greatest auditory threshold difference at 3000 Hz when compared to 2000 Hz, 4000 Hz, and 6000 Hz. A statistically significant gender by frequency interaction was also observed. Females had generally larger DPOAE absolute amplitude differences than males except at 4980

Hz. Additionally, a statistically significant gender by ear interaction was also observed. Females had significantly larger DPOAE absolute amplitude differences in the left ear versus males while males had significantly larger DPOAE absolute amplitude differences in the right ear versus the left.

## CHAPTER V: EXPERIMENT 4 – THE EFFECT OF NOISE EXPOSURE ON ELECTROCOCHLEOGRAPHY

It is well known that ECochG is a test used to investigate cochlear function (Ferraro, 2010; Ferraro & Tibbils, 1999; Ferraro et al., 1994; Nam & Won, 2004). The intertest reproducibility of ECochG recorded by extratympanic electrodes is good with relatively small changes in ECochG parameters (Nam & Won, 2004). As revealed in Experiment 1, the same can be said for ECochG recorded by Lilly TM-Wick electrodes. The Lilly TM-Wick electrodes do allow for larger responses resulting in more easily identified waveform components. Changes in ECochG indices have been reported for inner ear diseases including Ménière's disease. Results are inconsistent, however, for other inner ear diseases (Nam & Won, 2004). Nam and Won (2004) suggest that the SP/AP amplitude ratio is useful for early detection and monitoring of NIHL. Kim et al. (2005) suggest that ECochG provides more sensitive and specific information than DPOAEs for detecting a noise-induced TTS. Both of these studies utilized extratympanic recording techniques and uncontrolled noise stimuli. Gender effects and SP/AP area ratio were also not evaluated. The aim of Experiment 4 was to compare SP amplitude, AP latency, AP amplitude, SP/AP amplitude ratio, and SP/AP area ratio as a function of test and gender.

### **Methods**

#### **Participants**

Participants were the same 32 normal hearing young adults described in Experiments 2 and 3. Briefly, they were sixteen adult males with a mean age of 25.4 ( $SD = 2.9$ ) years and 16 adult females with a mean age of 24.0 ( $SD = 2.4$ ) years.

Participants were Caucasians with a negative history of loud noise exposure within 48 hours prior to data collection and no significant history of neurological, otological, and/or communication disorders. In examining the effect of noise exposure on DPOAEs, one ear was tested on each participant – with right and left ears counterbalanced - for a total of 32 ears. All participants had normal hearing sensitivity defined as pure tone thresholds at octave frequencies from 250 Hz to 8000 Hz  $\leq$  15 dB HL (American National Standards Institute, 2010). Participants also had normal middle ear function defined as  $Y_{tm} = 0.3\text{-}1.50$  mmho,  $TW = 35.80\text{-}95.00$  daPa,  $V_{ea} = 0.9\text{-}1.80$  cm<sup>3</sup>, and  $TPP \pm 50$  daPa (Roup et al., 1998; Marshall, Heller, & Westhusin, 1997). Mean hearing thresholds for all participants as a function of frequency, ear, and gender were displayed in Table 24 and mean tympanometric indices for all participants as a function of ear and gender were displayed in Table 26. In addition, participants were also required to have replicable ECochG responses to a 100  $\mu$ s click stimuli presented at 90 dB nHL in at least one ear.

## **Apparatus**

A GSI 61™ audiometer was utilized to obtain behavioral thresholds and tympanometric measures were obtained using a GSI TympStar™. The GSI 61™ audiometer was also the source for the 105 dBA 2000 Hz narrowband noise stimuli eliciting the TTS. ECochG data acquisition was performed using the IHS Smart EP evoked potential system. Lilly TM-Wick electrodes were utilized to record responses and muscle artifact for signal averaging techniques. All stimuli were presented via ER-3A insert earphones. A double-walled, sound treated audiometric test room (Industrial



Acoustics Corporation), meeting specifications for permissible ambient noise (American National Standards Institute, 1999), served as the test environment.

### **Experimental Signal**

ECochG responses were obtained to 100  $\mu$ s click stimuli of alternating polarity. The clicks were presented at 90 dB nHL with a slow rate (7.7 pulses per second) and 1,024 sweeps were averaged. The amplitude as a function of time waveforms for electric and acoustic click stimuli of condensation and rarefaction polarity were presented in Figures 2 through 5. FFTs on the alternating polarity electric and acoustic click were presented in Figures 6 and 7. The 2000 Hz narrowband noise stimulus calibration was performed as described above in Chapter III.

### **Electrophysiological Waveform Analysis**

The SP waveform component was analyzed in terms of amplitude and the AP waveform component was analyzed in terms of amplitude and latency. The SP/AP amplitude ratio and SP/AP area ratio were also calculated and analyzed. The baseline of the response was identified at the onset of the initial negative deflection of the SP and the AP was the first negative going peak after one millisecond (Ferraro & Tibbils, 1999; Ferraro, 2010). The SP was defined as the highest point of the shoulder of the ascending portion of the response, or the leading edge of the AP (Moon et al., 2012). Amplitudes were measured from the component trough to the baseline. The SP/AP area ratio was calculated in the IHS Smart EP system in accordance with recommendation from IHS by marking the amplitude of the base at the point in time following the AP trough where the response passed through the initial baseline amplitude.

## **Procedure**

The University and Medical Center Institutional Review Board at East Carolina University approved this research study prior to data collection or participant recruitment (see Appendix A). Participants were recruited from the East Carolina University student body to include the School of Allied Health Sciences as well as the Department of Communication Sciences and Disorders. Participants were recruited on a volunteer basis and an informed consent was reviewed and signed by each participant prior to data collection. All participants were required to meet the previously discussed inclusion criteria. During the recruiting and data collection process, funding through the East Carolina University Department of Communication Sciences and Disorders became available. Approval was obtained through the University and Medical Institutional Review Board at East Carolina University to implement this change. The allotted funds totaled \$700.00 and were distributed in \$5.00 merchandise gift cards. Thirty-two participants were paid a stipend of \$20.00 for participating in this investigation. Twelve participants were paid a stipend of \$5.00 due to the fact that they did not meet inclusion criteria and were consequently removed from data collection. The participants that received compensation signed a separate informed consent prior to data collection (see Appendix C).

Intake questions were answered prior to any data collection. Otoscopy was performed to verify clear external auditory canals and visualize normal TM landmarks. Pre-exposure behavioral thresholds were obtained by a co-investigator using the procedure recommended by ASHA (2005). The principle investigator was blind to the pre-exposure thresholds.

Baseline ECoGgs were then obtained using the following procedure. ECoGgs were recorded with Lilly TM-Wick electrodes with at least one replication. Participants were comfortably seated in a recliner in a quiet exam room for all conditions. Test ear was counterbalanced according to a digram-balanced Latin squares design (Wagenaar, 1969). Prior to data collection Signa-Gel® Electrode Gel was applied to the Lilly TM-Wick electrodes. These were then soaked in a saline solution for ten minutes. Participants were instructed to sit quietly with little movement throughout the test. A horizontal recording montage was utilized with the noninverting electrode on the lateral surface of the TM, the inverting electrode on the contralateral mastoid, and the ground electrode on  $F_{pz}$ . The skin was cleaned prior to electrode application by gently scrubbing NuPrep skin prep gel on  $F_{pz}$  as well as the contralateral mastoid. Lilly TM-Wick placement was verified by having the participant report when they heard the electrode bump against the TM, at which time the electrode lead was carefully taped anteroinferior to the intertragal notch and held while an insert earphone was placed into each participant's test ear so the outer portion was even with the canal, and held there until the foam tip had time to expand in the ear canal. Interelectrode impedances were kept at or below 7,000  $\Omega$ . The recorded EEG was amplified 100,000 times and bandpass filtered (10 to 1,500 Hz). Each recording contained 1,024 samples that were averaged and replicated for a rate of 7.7/s.

Participants were then exposed binaurally to a 2000 Hz narrowband noise presented at 105 dBA for ten minutes. Immediately following exposure, behavioral threshold testing was completed. For behavioral threshold testing, the four frequencies (i.e., 2000 Hz, 3000 Hz, 4000 Hz, 6000 Hz) were counterbalanced and thresholds were

obtained using the procedure recommended by ASHA (2005). Immediately following, post exposure ECoChG recordings were obtained using the procedure described above. Due to the Signa-Gel® Electrode Gel and saline solution on the Lilly-TM Wick electrodes, behavioral thresholds were obtained prior to ECoChG recordings for baseline and post exposure testing on every participant. This data was collected at the same time Experiment 3 data was collected. DPOAE testing and ECoChG testing were always performed on different ears so to avoid any effect of the gel and saline solution on the backwards transmission of the DPOAE response.

## **Results**

All descriptive and inferential analyses were conducted with IBM SPSS Statistics for Mac (Version 23.0.0.0). Means and standard deviations for ECoChG indices as a function of test, gender, and ear are displayed in Tables 51 to 54. Signed differences in SP amplitude, AP latency, AP amplitude, SP/AP amplitude ratio, and SP/AP area ratio were calculated by subtracting the post-noise exposure ECoChG indices from their respective pre-noise exposure ECoChG indices. Positive and negative differences reflect decreases and increases, respectively in ECoChG indices. Five separate two-factor univariate ANOVAs were performed to examine SP amplitude, AP latency, AP amplitude, SP/AP amplitude ratio, and SP/AP area ratio differences as a function of gender and ear. Results for each dependent variable will be discussed below.

### **SP Amplitude**

Boxplots (Figures 55 and 56) were constructed to visualize data and check the assumption of normalcy. A two-factor univariate ANOVA was conducted to examine SP amplitude differences as a function of gender and ear. The ANOVA summary for SP

Table 51. Mean Male Baseline ECoG Indices as a Function of Ear.

		SP Amplitude	AP Latency	AP Amplitude	SP/AP Amplitude Ratio	SP/AP Area Ratio
		( $\mu$ V)	(ms)	( $\mu$ V)	( $\mu$ V)	( $\mu$ V)
Baseline						
Right	<i>M</i>	0.2	1.7	0.6	0.4	0.6
	( <i>SD</i> )	(0.1)	(0)	(0.2)	(0.2)	(0.2)
	<i>N</i>	8	8	8	8	8
Left	<i>M</i>	0.2	1.7	0.7	0.3	0.5
	( <i>SD</i> )	(0.1)	(0.1)	(0.4)	(0.1)	(0.2)
	<i>N</i>	8	8	8	8	8

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

Table 52. Mean Male Post Exposure ECochG Indices as a Function of Ear.

		SP Amplitude	AP Latency	AP Amplitude	SP/AP Amplitude Ratio	SP/AP Area Ratio
		( $\mu$ V)	(ms)	( $\mu$ V)	( $\mu$ V)	( $\mu$ V)
Post						
Exposure						
Right	<i>M</i>	0.4	1.7	0.9	0.4	0.6
	( <i>SD</i> )	(0.4)	(0.1)	(0.8)	(0.2)	(0.2)
	<i>N</i>	8	8	8	8	8
Left	<i>M</i>	0.2	1.7	0.8	0.3	0.5
	( <i>SD</i> )	(0.1)	(0.1)	(0.3)	(0.1)	(0.2)
	<i>N</i>	8	8	8	8	8

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

Table 53. Mean Female Baseline ECochG Indices as a Function of Ear.

		SP Amplitude	AP Latency	AP Amplitude	SP/AP Amplitude Ratio	SP/AP Area Ratio
		( $\mu$ V)	(ms)	( $\mu$ V)	( $\mu$ V)	( $\mu$ V)
Baseline						
Right	<i>M</i>	0.3	1.7	1.0	0.3	0.6
	( <i>SD</i> )	(0.3)	(0.1)	(0.5)	(0.1)	(0.1)
	<i>N</i>	8	8	8	8	8
Left	<i>M</i>	0.1	1.6	0.6	0.3	0.5
	( <i>SD</i> )	(0)	(0.1)	(0.2)	(0.1)	(0.1)
	<i>N</i>	8	8	8	8	8

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.

Table 54. Mean Female Post Exposure ECochG Indices as a Function of Ear.

		SP Amplitude ( $\mu$ V)	AP Latency (ms)	AP Amplitude ( $\mu$ V)	SP/AP Amplitude Ratio ( $\mu$ V)	SP/AP Area Ratio ( $\mu$ V)
Post						
Exposure						
Right	<i>M</i>	0.2	1.7	0.8	0.3	0.5
	( <i>SD</i> )	(0.1)	(0.1)	(0.2)	(0.1)	(0.1)
	<i>N</i>	8	8	8	8	8
Left	<i>M</i>	0.3	1.6	0.7	0.4	0.6
	( <i>SD</i> )	(0.1)	(0.1)	(0.3)	(0.1)	(0.1)
	<i>N</i>	8	8	8	8	8

*Note.* Values enclosed in parentheses represent one standard deviation of the mean.



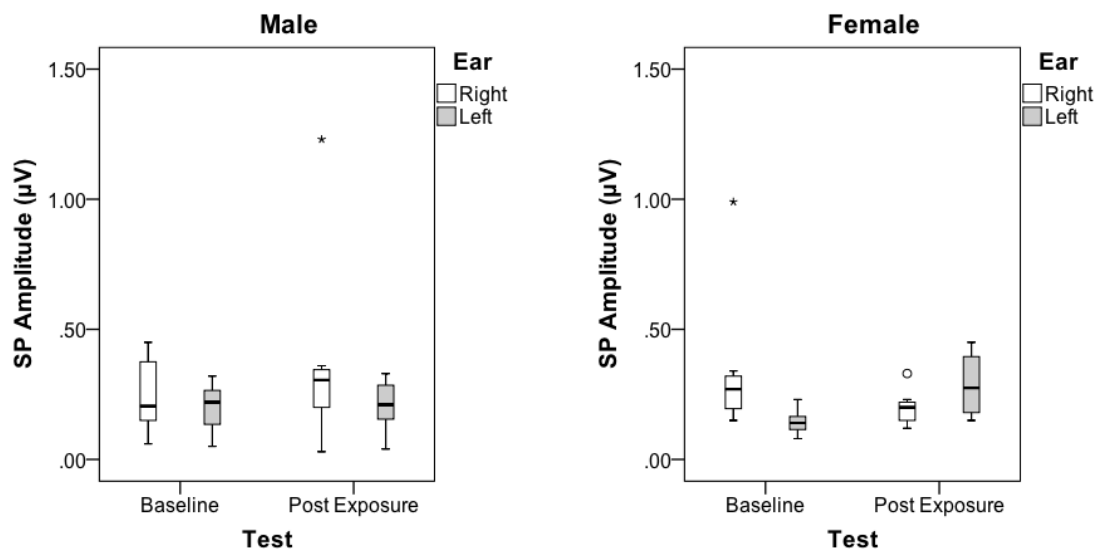
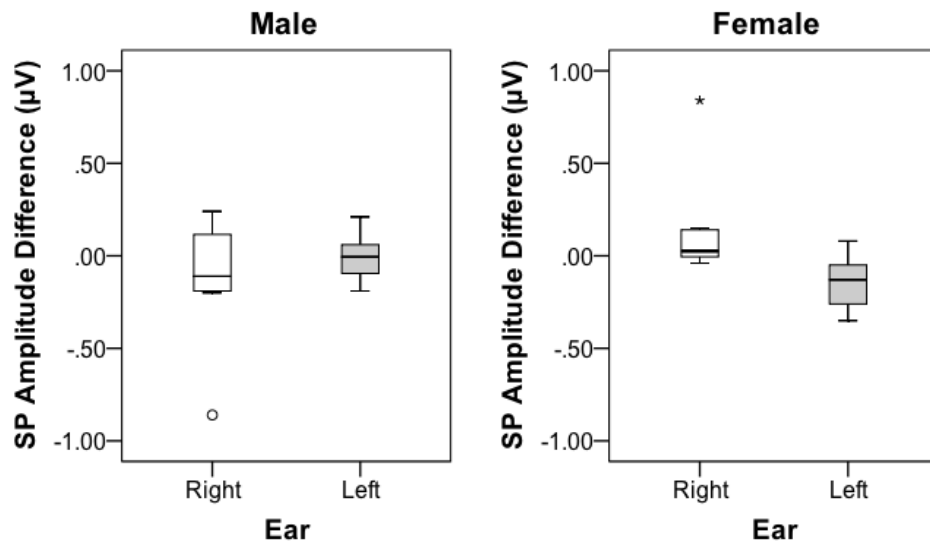


Figure 55. Boxplots of SP amplitude as a function of test, gender, and ear. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).



*Figure 56.* Boxplots of SP amplitude differences as a function of gender and ear. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

amplitude is presented in Table 55. There was a statistically significant interaction of ear and gender ( $p < .05$ ). Four independent  $t$ -tests were undertaken to find the source of the interaction (Table 56). As evident in Table 56, SP amplitudes were significantly increased for female left ears following noise exposure than for female right ears.

### **AP Latency**

Boxplots (Figures 57 and 58) were constructed to visualize data and check the assumption of normalcy. A two-factor univariate ANOVA was conducted to examine AP latency differences as a function of gender and ear. The ANOVA summary for AP latency is presented in Table 57. There were no statistically significant main effects or interactions on AP latency ( $p > .05$ ).

### **AP Amplitude**

Boxplots (Figure 59 and 60) were constructed to visualize data and check the assumption of normalcy. A two-factor univariate ANOVA was conducted to examine AP amplitude differences as a function of gender and ear. The ANOVA summary for AP amplitude is presented in Table 58. There were no statistically significant main effects or interactions on AP amplitude ( $p > .05$ ).

### **SP/AP Amplitude Ratio**

Boxplots (Figures 61 and 62) were constructed to visualize data and check the assumption of normalcy. A two-factor univariate ANOVA was conducted to examine SP/AP amplitude ratio differences as a function of gender and ear. The ANOVA summary for SP/AP amplitude ratio is presented in Table 59. A statistically significant main effect of ear ( $p < .05$ ) was found. No statistically significant main effect of gender was seen and no statistically significant interaction was found ( $p > .05$ ). Left ear SP/AP

Table 55. *Summary of Two-Factor Univariate ANOVA Comparing SP Amplitude Differences (in  $\mu\text{V}$ ) as a Function of Gender and Ear.*

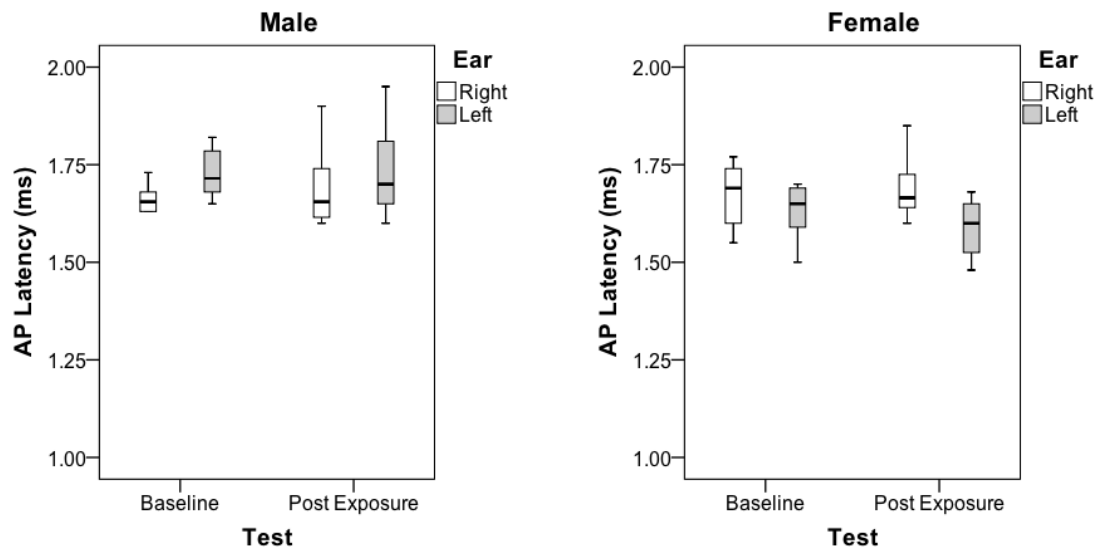
Source	Sum of Squares	<i>df</i>	Mean Square	<i>F</i>	<i>p</i>	$\eta_p^2$
Gender	0.03	1	0.03	0.55	.46	.02
Ear	0.06	1	0.03	0.95	.34	.03
Gender X Ear	0.32	1	0.06	.5.44	.03*	.16

*Note.* *N* = 32 for ANOVA; \*statistically significant at  $p < .05$ ; <sup>a</sup>Greenhouse-Geisser value.

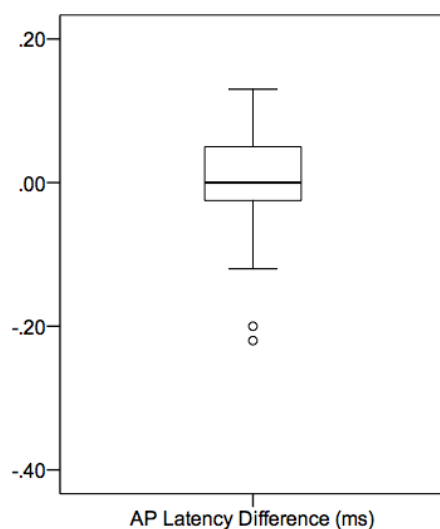
Table 56. *Summary of Independent-Samples t-tests Examining the Interaction of Gender and Ear on SP Amplitude Differences (in  $\mu V$ ).*

Pair	Paired Differences						
	95% CI of the Difference				<i>t</i>	<i>df</i>	<i>p</i>
	Mean Difference	<i>SE Difference</i>	Lower	Upper			
Female Right vs. Female Left	0.28	0.11	0.04	0.53	2.48	14	.03*
Male Right vs. Male Left	-0.12	0.13	-0.39	0.16	-0.91	14	.38
Female Right vs. Male Right	0.26	0.16	-0.07	0.60	1.67	14	.12
Female Left vs. Male Left	-0.14	0.07	-0.28	0.01	-2.02	14	.06

*Note.* *N* = 16 for *t*-tests; \*statistically significant at  $p < .05$ .



*Figure 57.* Boxplots of AP latency as a function of test, gender, and ear. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).



*Figure 58.* Boxplot of AP latency differences (in ms) collapsed across gender and ear.

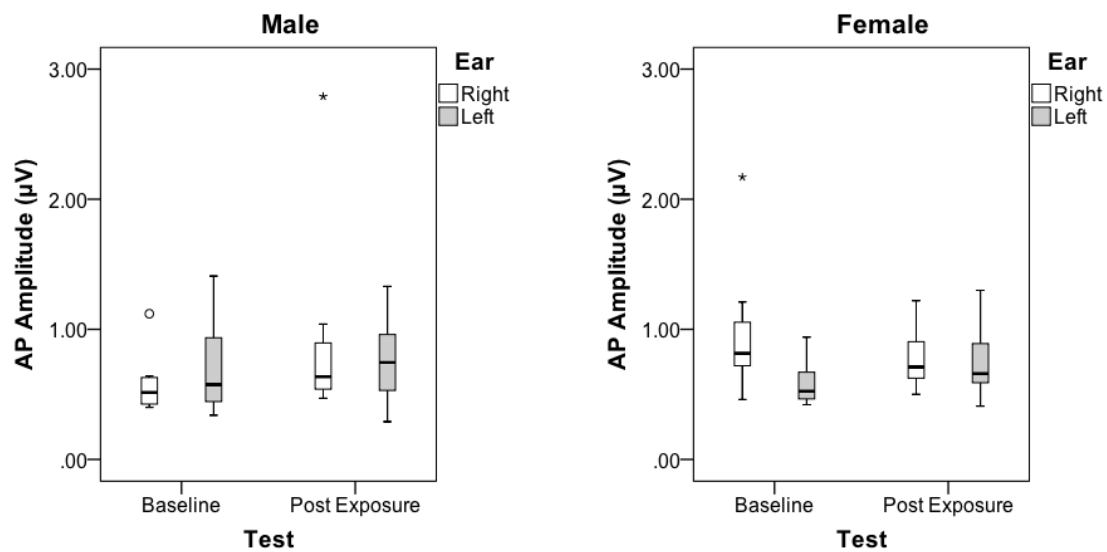
The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

Table 57. *Summary of Two-Factor Univariate ANOVA Comparing AP Latency Differences (in ms) as a Function of Gender and Ear.*

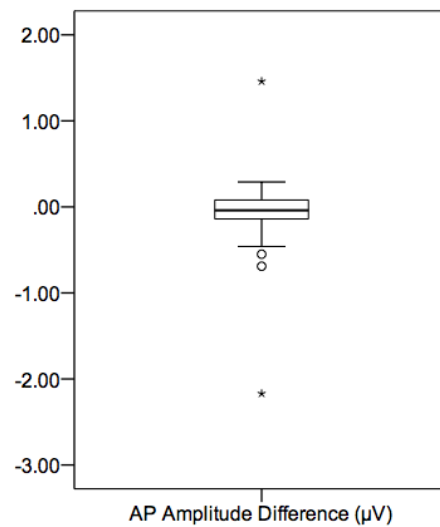
Source	Sum of Squares	<i>df</i>	Mean Square	<i>F</i>	<i>p</i>	$\eta_p^2$
Gender	0.01	1	0.01	1.45	.24	.05
Ear	0.01	1	0.01	2.71	.11	.09
Gender X Ear	0.00	1	0.00	0.51	.48	.02

*Note.* *N* = 32 for ANOVA; \*statistically significant at  $p < .05$ ; <sup>a</sup>Greenhouse-Geisser value.





*Figure 59.* Boxplots of AP amplitude as a function of test, gender, and ear. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).



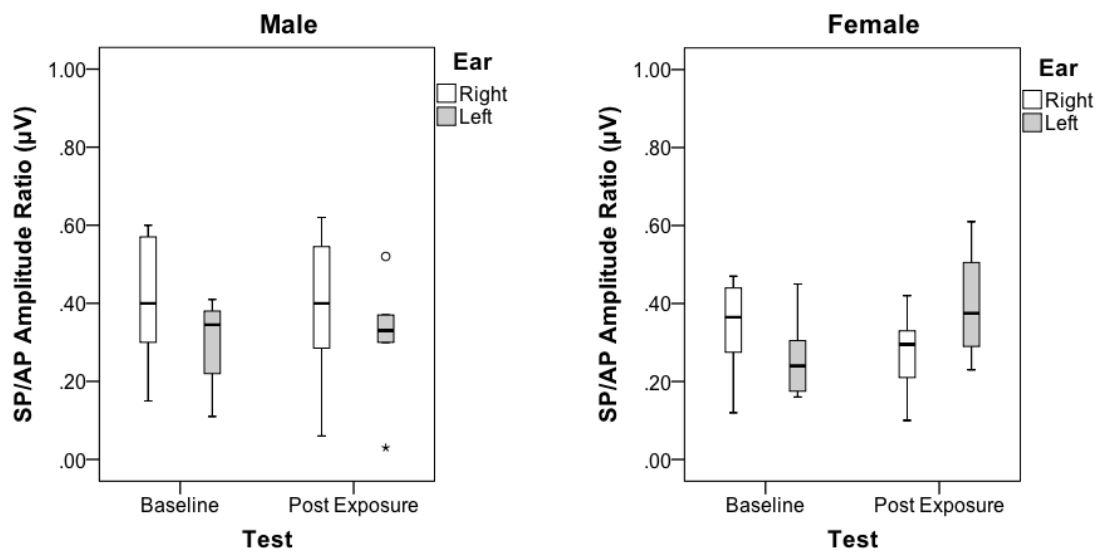
*Figure 60.* Boxplot of AP amplitude differences (in  $\mu\text{V}$ ) collapsed across gender and ear.

The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

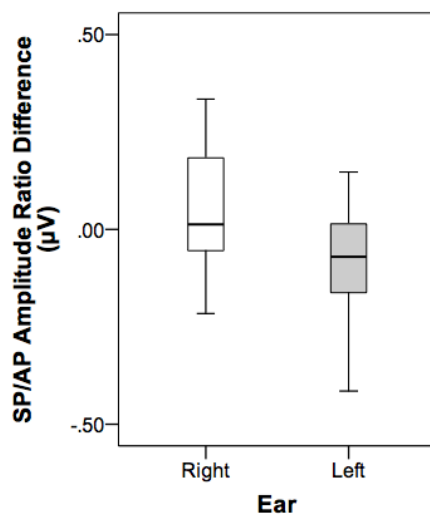
Table 58. *Summary of Two-Factor Univariate ANOVA Comparing AP Amplitude Differences (in  $\mu\text{V}$ ) as a Function of Gender and Ear.*

Source	Sum of Squares	<i>df</i>	Mean Square	<i>F</i>	<i>p</i>	$\eta_p^2$
Gender	0.38	1	0.38	1.54	.23	.05
Ear	0.01	1	0.01	0.05	.83	.00
Gender X Ear	0.86	1	0.86	3.50	.07	.11

*Note.* *N* = 32 for ANOVA; \*statistically significant at  $p < .05$ ; <sup>a</sup>Greenhouse-Geisser value.



*Figure 61.* Boxplots of SP/AP amplitude ratio as a function of test, gender, and ear. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).



*Figure 62.* Boxplots of SP/AP amplitude ratio differences (in  $\mu\text{V}$ ) as a function of ear.

The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

Table 59. *Summary of Two-Factor Univariate ANOVA Comparing SP/AP Amplitude Ratio Differences (in  $\mu\text{V}$ ) as a Function of Gender and Ear.*

Source	Sum of Squares	<i>df</i>	Mean Square	<i>F</i>	<i>p</i>	$\eta_p^2$
Gender	0.01	1	0.01	0.48	.50	.02
Ear	0.12	1	0.12	5.25	.03*	.16
Gender X Ear	0.06	1	0.06	2.67	.11	.09

*Note.* *N* = 32 for ANOVA; \*statistically significant at  $p < .05$ ; <sup>a</sup>Greenhouse-Geisser value.

amplitude ratios increased following noise exposure while right ear SP/AP amplitude ratios showed essentially no difference following noise exposure.

### **SP/AP Area Ratio**

Boxplots (Figure 63 and 64) were constructed to visualize data and check the assumption of normalcy. A two-factor univariate ANOVA was conducted to examine SP/AP area ratio differences as a function of gender and ear. The ANOVA summary for SP/AP area ratio is presented in Table 60. A statistically significant main effect of ear ( $p < .05$ ) was found. No statistically significant main effect of gender was seen and no statistically significant interaction was found ( $p > .05$ ). Left ear SP/AP area ratios increased following noise exposure while right ear SP/AP area ratios showed essentially no difference following noise exposure.

### **Discussion**

The aim of the fourth experiment was to examine the effect of noise on SP amplitude, AP latency, AP amplitude, SP/AP amplitude ratio, and SP/AP area ratio in young adults. The overall hypotheses were that there would be no statistically significant main effects of ear or gender and no significant interaction. More specifically, it was hypothesized that there would be a significant decrease in AP amplitude, increase in SP amplitude, increase in AP latency, and increase in SP/AP amplitude ratio following noise exposure. It was not anticipated that there would be a change in SP/AP area ratio. Contrary to the hypotheses, the only main effect found was that of ear for SP/AP amplitude ratio and SP/AP area ratio. For both of these ratios, the left ear response differences were statistically larger while there was essentially no difference for right ear responses. Additionally, there was a significant ear by gender interaction

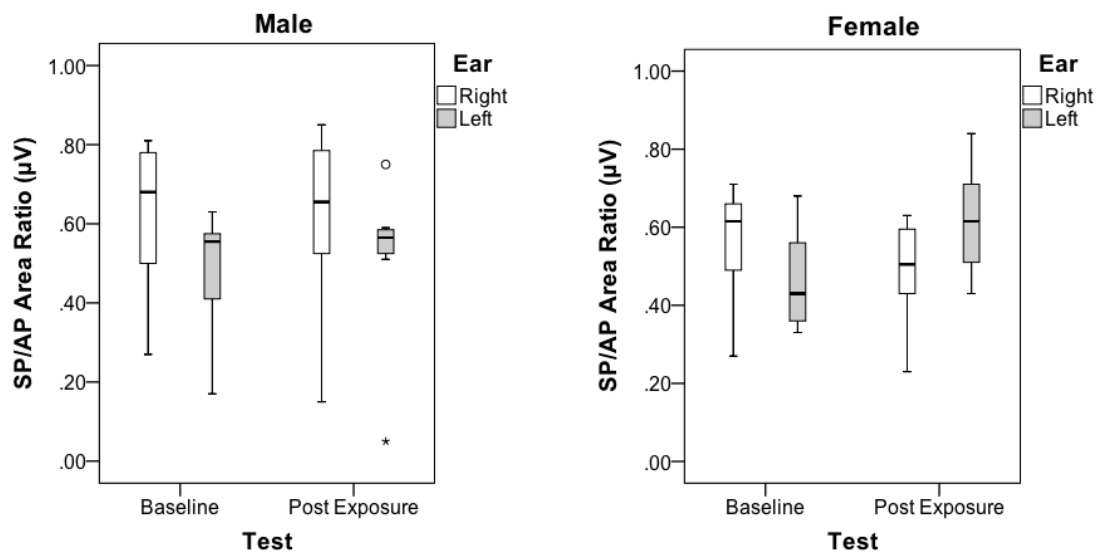
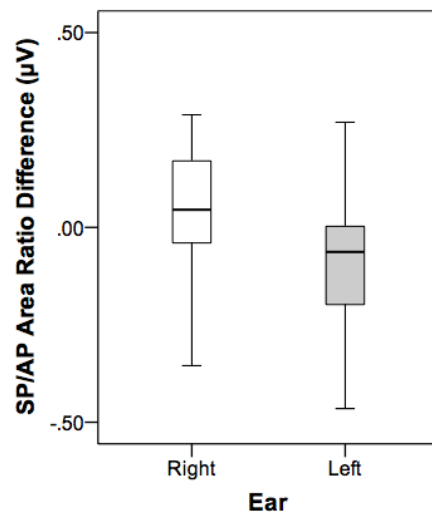


Figure 63. Boxplots of SP/AP area ratio as a function of test, gender, and ear. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).





*Figure 64.* Boxplots of SP/AP area ratio differences (in  $\mu\text{V}$ ) as a function of ear. The top, bottom, and line through the middle of the box denote the 75th, 25th, and 50th percentile (median) respectively. Circles denote outliers (i.e., cases with values between 1.5 and 3 times the interquartile range). Asterisks denote extreme outliers (i.e., cases with values greater than three times the interquartile range).

Table 60. *Summary of Two-Factor Univariate ANOVA Comparing SP/AP Area Ratio Differences (in  $\mu\text{V}$ ) as a Function of Gender and Ear.*

Source	Sum of Squares	<i>df</i>	Mean Square	<i>F</i>	<i>p</i>	$\eta_p^2$
Gender	0.01	1	0.01	0.22	.64	.01
Ear	0.15	1	0.15	4.67	.04*	.14
Gender X Ear	0.07	1	0.07	2.14	.16	.07

*Note.* *N* = 32 for ANOVA; \*statistically significant at  $p < .05$ ; <sup>a</sup>Greenhouse-Geisser value.

for SP amplitude. There was a larger response difference for female left ears than for female right ears.

The results of this study differ slightly from previous studies. Nam and Won (2004) found that the SP amplitude and SP/AP amplitude ratio increased significantly following three hours of consecutive noise exposure in a commercial computer-game arcade. No changes were noted for AP amplitude. Kim et al. (2005) found similar results following two consecutive hours of music in a night-club. Their study identified significant main effects of SP amplitude, SP/AP amplitude ratio, and AP duration. Neither of these studies evaluated SP/AP area ratio changes. Kim et al. (2005) found that ECoG appears to provide more sensitive and specific information than DPOAEs for detecting a noise-induced TTS. The current findings from Experiment 4 are suggestive of the left ear being more susceptible to effects of noise, especially for females. The slight differences in results from this study compared to Nam and Won (2004) and Kim et al. (2005) could be attributed to the different eliciting stimulus for TTS and the different electrode types. The noise exposure was less controlled in the previously mentioned studies; however, the exposure time was significantly longer than for Experiment 4. Polyurethane foam tips wrapped in gold foil were utilized as the recording electrode rather than Lilly TM-Wick electrode placed on the lateral surface of the TM.

## CHAPTER VI: GENERAL DISCUSSION

As discussed previously, noise exposure is the second leading cause of hearing loss after age-related hearing loss and is one of the most common occupational and environmental hazards (Rabinowitz, 2000). In addition, noise exposure is also the most preventable contribution to hearing loss in the United States (Dobie, 2008). More than 30 million Americans are exposed to potentially harmful noise levels each day in the workplace and even more Americans are affected by harmful noise levels in their recreational activities (Rabinowitz, 2000). The NIDCD reports that approximately 26 million Americans have some degree of NIHL (NIDCD, 2014). This equates to roughly 15% of Americans between the ages of 20 and 69 as well as 16% of teenagers between 12 and 19 years of age.

Noise exposure can cause either temporary or permanent damage and is either the result of a one-time exposure to an intense noise or continuous exposure to loud sounds over an extended period of time. With proper regulations as provided by OSHA, NIHL is completely preventable. The noise contributing to a TTS has no morphological effect on the cochlea but can be attributed to metabolic changes with the outer hair cells of the cochlea, which are essential to hearing sensitivity and frequency selectivity and can be observed in the electrical response of the outer hair cells in the cochlea or by measuring changes to otoacoustic emission responses (Patuzzi, 1998; Quaranta et al., 2003). TTSs have been utilized as a safe test of susceptibility to PTS (Yates, Cody, & Johnstone, 1983). The purpose of this study was to examine effects of short term noise exposure on auditory function including behavioral thresholds, DPOAEs, and ECochG indices.

## Summary of Experimental Findings

### Comparing Two Electrodes in Terms of Reliability and Rate in Young Adults

Prior to the evaluation of the effect of noise on ECoChG, it was necessary to determine the appropriate electrode and stimulus types for replicable and identifiable waveforms. Test-retest reliability was examined with correlation coefficients, linear mixed model analyses of variance, test-retest differences, and Bland-Altman plots. This is the first report of reliability of ECoChG responses recorded with both Lilly TM-Wick and TIPtrode™ electrodes at slow and fast stimulus rates. It was hypothesized that there would be no effect of test but that there would be an effect of electrode type and rate on ECoChG indices. Responses recorded with Lilly TM-Wick electrodes were hypothesized to have a significantly larger amplitude than those obtained with a TIPtrode™ electrodes. It was also hypothesized that the faster rate of 77.7/s would result in longer latencies, smaller amplitudes, and larger SP/AP amplitude and area ratios.

Initially, electrode ( $p < .001$ ) and rate ( $p = .001$ ) were found to be statistically significant predictors for the presence of an ECoChG response. A response was more apt to be present when recorded with a Lilly TM-Wick electrode and at a slow rate of 7.7/s. When utilizing Lilly TM-Wick electrodes, statistically significant Pearson's product-moment correlations between initial test and retest were found for all ECoChG indices ( $p < .05$ ; SP amplitude, AP latency, AP amplitude, SP/AP amplitude ratio, and SP/AP area ratio). All ECoChG indices, except for SP amplitude, showed statistically significant correlations ( $p < .05$ ) between initial test and retest when recording with TIPtrodes™.

A statistically significant main effect of electrode was noted for SP amplitude ( $p < .001$ ), AP amplitude ( $p < .001$ ), and SP/AP amplitude ratio ( $p < .001$ ). For each of these indices the amplitude was larger when recording with Lilly TM-Wick electrodes as anticipated. A statistically significant main effect of rate was identified for SP amplitude ( $p < .05$ ), AP latency ( $p < .001$ ), AP amplitude ( $p < .05$ ), SP/AP amplitude ratio ( $p < .001$ ), and SP/AP area ratio ( $p < .001$ ). SP amplitudes were statistically larger for the faster rate of 77.7/s than for the slower rate of 7.7/s. AP latency was statistically longer for the faster rate of 77.7/s. AP amplitudes were statistically larger for the slower rate of 7.7/s. Both SP/AP amplitude ratio and SP/AP area ratio were statistically larger for the fast rate of 77.7/s. There was no statistically significant effect of test on any ECoG indices ( $p > .05$ ). These findings were also in agreement with the initial hypotheses.

A number of outliers were noted with all five ECoG indices. This was particularly evident with amplitude measures (Hall, 2007). Amplitude measures are prone to more variability than latency measures due to the likelihood of electrical noise contamination – both extraneous environmental activity (e.g., 60 Hz interference) and internal (participant) ongoing neurogenic and myogenic activity.

Due to the test-retest reliability demonstrated in this study and the potential for easier identification of ECoG wave components, Lilly-TM Wick electrodes were deemed superior to TIPtrode™ electrodes for recording ECoG. In addition, responses were more apt to be present when recording with Lilly-TM Wick electrodes. Similarly, responses are more apt to be present when using a slow stimulus rate of 7.7/s. Due to these findings, ECoG recordings in Experiment 4 were obtained with Lilly-TM Wick electrodes and a slow stimulus rate of 7.7/s.

## Differences in Behavioral Thresholds Following Noise Exposure in Young Adults

In Experiment 2, it was hypothesized that there would be observable threshold elevations for the audiogram following noise exposure. No main effects of gender, frequency, or ear were anticipated for auditory threshold; however, an interaction was expected with greater changes at certain frequencies (Kummer et al., 1998). It was conjectured that greater changes would occur around 3000 Hz (Engdahl & Kemp, 1996). As expected, there was no statistically significant main effect of gender ( $p > .05$ ) following noise exposure. Contrary to the hypotheses, statistically significant main effects of frequency ( $p < .0001$ ) and ear ( $p < .0001$ ) were found. Larger auditory threshold differences were observed for left ears than for right ears. As predicted, larger auditory threshold differences were identified for 3000 Hz than 2000 Hz, 4000 Hz or 6000 Hz. In addition, statistically significant Pearson's product-moment correlations were found between right and left ear auditory threshold differences at 3000 Hz ( $p < .0001$ ), 4000 Hz ( $p = .02$ ), and 6000 Hz ( $p < .0001$ ).

Acoustic reflex indices were also investigated in Experiment 2 to examine the association between auditory threshold differences and ipsilateral acoustic reflex threshold to a 2000 Hz pure tone and a 2000 Hz narrowband noise. In addition, the association between auditory threshold differences and acoustic reflex latency was also examined. Statistically significant Pearson's product-moment correlations between right ear auditory threshold difference at 3000 Hz and right 2000 Hz pure tone acoustic reflex threshold ( $p = .04$ ) as well as between left ear auditory threshold difference at 3000 Hz and left 2000 Hz pure tone acoustic reflex threshold ( $p = .03$ ) and 2000 Hz narrowband noise acoustic reflex threshold ( $p = .01$ ) were found. There were no statistically

significant correlations ( $p > .05$ ) between auditory threshold differences at any frequency for either ear and acoustic reflex latency.

Overall, the findings in Experiment 2 suggest that a 2000 Hz narrowband noise is adequate for eliciting auditory threshold differences in a limited region of the cochlea. The greatest effect was seen at 3000 Hz, which is approximately  $\frac{1}{2}$ -octave above the eliciting stimulus. This is similar to previous research (Ward, 1973; Melnick, 1978; Engdahl & Kemp, 1996; Hooks-Horton et al., 2001). Research on gender effects for auditory threshold differences is equivocal. Similar to the results from this study, Pirilä (1991a, b) also found that good hearing thresholds in the right ear seem to be better protected from noise-induced auditory threshold differences than good hearing thresholds in the left ear. Hooks-Horton et al. (2001) failed to find a significant effect of gender on auditory threshold differences.

Interestingly, ipsilateral 2000 Hz pure tone acoustic reflex thresholds were significantly correlated with auditory threshold differences at 3000 Hz for both ears. Ipsilateral 2000 Hz narrowband noise acoustic reflex thresholds were only correlated with left ear 3000 Hz auditory threshold difference. These results suggest that, when using a controlled 2000 Hz narrowband noise to elicit an auditory threshold difference, participants with higher acoustic reflex thresholds tended to have a greater auditory threshold difference at 3000 Hz. The premise supports the theory that the acoustic reflex provides inner ear protection from noise damage. This notion has also been challenged (Aiken et al., 2013; Phillips, Stuart, & Carpenter, 2002). There was no relationship between acoustic reflex latency measures and auditory threshold differences.



## Differences in DPOAEs Following Noise Exposure in Young Adults

The hypothesis of the third experiment was that DPOAE absolute amplitudes would be decreased following noise exposure with the greatest effects being seen at low L1, L2 levels. No effects of gender, ear, or frequency were anticipated for DPOAE I/O functions; however, an interaction was expected with greater changes at certain frequencies. Statistically significant main effects of level ( $p < .0001$ ) and frequency ( $p < .0001$ ) were observed. DPOAE absolute amplitude differences were statistically different for each level ( $p < .05$ ). As hypothesized, DPOAE absolute amplitude differences were largest for the L1, L2 level of 55, 40 dB SPL and smallest for the L1, L2 level of 65, 65 dB SPL. Regarding frequency, DPOAE absolute amplitude differences for 2051 Hz were statistically different from the other three  $f_2$  frequencies ( $p < .05$ ). DPOAE absolute amplitude differences were smallest for the  $f_2$  frequency of 2051 Hz. Finally, two interactions were observed. A statistically significant gender by frequency interaction ( $p < .05$ ) was identified. Females generally had larger DPOAE absolute amplitude differences than males except at the  $f_2$  frequency of 4980 Hz. Additionally, a statistically significant gender by ear interaction was also observed. Females had significantly larger DPOAE absolute amplitude differences in the left ear versus males while males had significantly larger DPOAE absolute amplitude differences in the right ear versus the left.

The findings of Experiment 3 suggest that DPOAE I/O functions are sensitive to cochlear changes that occur during an auditory threshold difference elicited by a 2000 Hz narrowband noise stimulus. Engdahl and Kemp (1996), utilizing the same eliciting noise, found that following noise exposure there was a greater change in absolute

amplitude at low stimulus levels. Similar results were identified in this study as well. Results from this study in congruence with those of Engdahl and Kemp (1996) support the notion that DPOAE low primary levels are indicated in DPOAE use as a safe and sensitive monitor of susceptibility to noise.

### **Differences in ECoChG Indices Following Noise Exposure in Young Adults**

In Experiment 4, it was hypothesized that there would be a decrease in AP amplitude, increase in SP amplitude, AP latency, and SP/AP amplitude ratio, and no change in SP/AP area ratio following noise exposure. No effects of gender and no interactions were anticipated.

For SP amplitude differences, a statistically significant interaction of ear and gender ( $p < .05$ ) was found. SP amplitudes were significantly increased for female left ears following noise exposure while female right ears showed essentially no change. There were no statistically significant main effects or interactions on AP latency or AP amplitude ( $p > .05$ ). Similar results were found for both SP/AP amplitude ratio and SP/AP area ratio. A statistically significant main effect of ear ( $p < .05$ ) was found for both ECoChG ratios. No statistically significant main effect of gender ( $p > .05$ ) was seen and no statistically significant interaction was found ( $p > .05$ ). Left ear SP/AP amplitude ratios and SP/AP area ratios increased following noise exposure while right ear SP/AP amplitude ratios and SP/AP area ratios showed essentially no difference following noise exposure.

Interestingly, the only significant main effect in any ECoChG indices following 10 minutes of a 2000 Hz narrowband noise was for the main effect of ear for SP/AP amplitude ratio and SP/AP area ratio. Additionally, there was a significant ear by

gender interaction for SP amplitude. AP latency and AP amplitude measures were unchanged following noise exposure. SP amplitudes for female left ears were significantly increased as were SP/AP amplitude and SP/AP area ratios for left ears only. Left ears were consistently more vulnerable to the effects of noise exposure than right ears. It is not surprising that SP/AP amplitude and area ratios were increased following noise exposure since SP amplitudes were increased. Experiment 4 results were similar to previous studies (Nam & Won, 2004; Kim et al., 2005). Nam and Won (2004) exposed participants to three consecutive hours in the same commercial computer-game arcade. Kim et al. (2005) exposed participants to music for two consecutive hours in the same night-club. In both studies, changes were noted for SP amplitude and SP/AP amplitude ratio. Kim et al. (2005) found that ECoChG appears to provide more sensitive and specific information than DPOAEs for detecting a noise-induced TTS. These studies did not examine gender effects and did not calculate SP/AP area ratios.

Overall, Experiments 2, 3, and 4 reveal that behavioral thresholds, DPOAE I/O functions, and ECoChG showed measureable changes following noise exposure resulting in an auditory threshold difference. The clinical implications of these findings will be discussed in detail below.

### **Clinical Implications**

The findings in this series of experiments provide additional support for early detection of cochlear changes as the result of noise exposure with behavioral thresholds, DPOAE I/O functions, and ECoChG. It appears that the cochlear changes as assessed by behavioral thresholds, DPOAE I/O functions, and ECoChG can be

observed following a controlled noise exposure (i.e., 2000 Hz narrowband noise at 105 dBA for ten minutes) as well as a real world exposure ([i.e., three consecutive hours in the same commercial computer-game arcade or music for two consecutive hours in the same night-club]; Nam & Won, 2004; Kim et al., 2005). DPOAE I/O functions do not seem to be sensitive to ear effects and, as a result, may be a better clinical tool to be used as a safe and sensitive monitor of susceptibility to noise.

Experiment 1 demonstrated test-retest reliability of the Lilly-TM Wick electrodes as well as easier to identify waveform components. However, it is difficult to verify placement with a Lilly-TM Wick. Placement is partially blind due to the TM being obscured by the electrode tip during the process (Ferraro, 2010). A subjective, and possibly false, response was obtained from the participants when they heard the electrode bump against the TM. In addition, it was noted that the cotton tip on the end of the electrode cable varied in size between the Lilly-TM Wick electrodes. This could result in greater or poorer TM contact depending on the surface area of the cotton tip. In addition, impedances were higher when recording on the surface of the TM compared to the ear canal. When recording with TIPtrodes™, the ear canal is scrubbed with NuPrep skin prep gel prior to electrode placement. Due to the recording site, this is not possible for Lilly-TM Wick recordings.

A similar clinical consideration is the expense of electrodes. TIPtrode™ electrodes are approximately \$3 per electrode. Lilly-TM Wick electrodes are much more expensive at approximately \$20 per electrode. When seeing many patients in a clinical setting the benefit versus the cost must be considered. As was discussed in

Experiment 1, TIPtrodes™ also demonstrate excellent test-retest reliability, are easier to verify placement, and are more affordable for clinical use.

### **Future Research Directions**

The results of this study support the notion that behavioral thresholds, DPOAE I/O functions, and ECochG are sensitive to cochlear changes as a result of short duration noise exposure; however, additional research is required to determine the usefulness of ECochG in assessing cochlear changes following noise exposure resulting in a TTS. It has been suggested that noise exposure induces increased  $\text{Ca}^{2+}$  concentration in the inner ear (Li et al., 2003; Ohashi et al., 2013). This would produce imbalance of  $\text{Ca}^{2+}$  homeostasis leading to an increase in osmotic pressure (Ohashi et al., 2013). The increased  $\text{Ca}^{2+}$  may also decrease the CM and endocochlear potential while increasing the SP. The increase in SP would then lead to enhanced SP/AP amplitude ratio and SP/AP area ratio. Future studies should evaluate why, as observed in this study, only the left ear showed effects of noise exposure in ECochG recordings.

There are also ethical considerations when evaluating the effects of noise exposure in humans. There must be a balance between exposing participants to a noise exposure in hopes of observing a TTS without eliciting a PTS. Research in mice has shown that acoustic noise exposure following moderate, but completely reversible, threshold elevation cause “acute loss of afferent nerve terminals and delayed degeneration of the cochlear nerve” (Kujawa & Liberman, 2009, p. 14077). The observed primary neurodegeneration can add to perceptual anomalies associated with inner ear hearing loss including tinnitus and difficulties hearing in noisy environments.

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# APPENDIX A: UNIVERSITY & MEDICAL CENTER INSTITUTIONAL REVIEW BOARD

## APPROVAL LETTER



**EAST CAROLINA UNIVERSITY**  
**University & Medical Center Institutional Review Board Office**  
4N-70 Brody Medical Sciences Building · Mail Stop 682  
600 Moye Boulevard · Greenville, NC 27834  
Office **252-744-2914** · Fax **252-744-2284** · [www.ecu.edu/irb](http://www.ecu.edu/irb)

### Notification of Initial Approval: Expedited

From: Biomedical IRB  
To: [Alyson Butler](#)  
CC: [Andrew Stuart](#)  
Date: 4/4/2013  
Re: [UMCIRB 12-002023](#)  
Noise exposure and auditory function

I am pleased to inform you that your Expedited Application was approved. Approval of the study and any consent form(s) is for the period of 3/18/2013 to 3/17/2014. The research study is eligible for review under expedited category #4. The Chairperson (or designee) deemed this study no more than minimal risk.

Changes to this approved research may not be initiated without UMCIRB review except when necessary to eliminate an apparent immediate hazard to the participant. All unanticipated problems involving risks to participants and others must be promptly reported to the UMCIRB. The investigator must submit a continuing review/closure application to the UMCIRB prior to the date of study expiration. The Investigator must adhere to all reporting requirements for this study.

The approval includes the following items:

Name	Description
<a href="#">Email.docx</a>   <a href="#">History</a>	Recruitment Documents/Scripts
<a href="#">Flyer.docx</a>   <a href="#">History</a>	Recruitment Documents/Scripts
<a href="#">Informed Consent.doc</a>   <a href="#">History</a>	Consent Forms
<a href="#">Protocol</a>   <a href="#">History</a>	Study Protocol or Grant Application

The Chairperson (or designee) does not have a potential for conflict of interest on this study.

## APPENDIX B: INFORMED CONSENT – NO PARTICIPANT COMPENSATION

Study ID:UMCIRB 12-002023 Date Approved: 3/18/2013 Expiration Date: 3/17/2014

East Carolina University



### Informed Consent to Participate in Research

Information to consider before taking part in research that has no more than minimal risk.

Title of Research Study: The effect of noise exposure on auditory threshold, otoacoustic emissions, and stimulus dependent cochlear potentials

Principal Investigator: Alyson K. Butler, B.S.

Institution/Department or Division: Department of Communication Sciences & Disorders, College of Allied Health Sciences, East Carolina University

Address: Greenville, NC 27858

Telephone #: 252-744-6113

Researchers at East Carolina University (ECU) study problems in society, health problems, environmental problems, behavior problems and the human condition. Our goal is to try to find ways to improve the lives of you and others. To do this, we need the help of volunteers who are willing to take part in research.

#### Why is this research being done?

The purpose of this research is to examine the effect of noise on inner ear function in normal-hearing young adults. Inner ear function can be tested noninvasively in humans through electrocochleography (ECochG) and distortion product otoacoustic emissions (DPOAEs). ECochG is an event related potential measuring electrical responses of the inner ear and auditory nerve. DPOAEs are sounds emitted following acoustic stimulation to short/brief duration stimulus. ECochG and DPOAEs provide simple, efficient, and non-invasive objective indicators of healthy inner ear function. The decision to take part in this research is yours to make. By doing this research, we hope to learn the effect of noise on inner ear function as assessed with ECochG and DPOAEs.

#### Why am I being invited to take part in this research?

You are being invited to take part in this research because you are a healthy young adult. If you volunteer to take part in this research, you will be one of 24 people to do so.

#### Are there reasons I should not take part in this research?

I understand I should not volunteer for this study if I do not have normal hearing, I am under 18 years of age, or I have been exposed to loud noise/sound in the last 48 hours.

#### What other choices do I have if I do not take part in this research?

You have the choice of not taking part in this research study.

#### Where is the research going to take place and how long will it last?

The research procedures will be conducted in the Department of Communication Sciences and Disorders, College of Allied Health Sciences, East Carolina University, Greenville, NC. You will need to come to room 2310H twice during the study. The total amount of time you will be asked to volunteer for this study is approximately three hours during two days over the next month.

UMCIRB Number: \_\_\_\_\_

Consent Version # or Date: \_\_\_\_\_

UMCIRB Version 2012.03.12

Participant's Initials

*Title of Study: The effect of noise exposure on auditory threshold, otoacoustic emissions, and stimulus dependent cochlear potentials*

**What will I be asked to do?**

You are being asked to do the following: First, you will receive a standard clinical audiometric hearing evaluation including tests called otoscopy, tympanometry, acoustic reflex testing, and audiometry (pure tone testing). Otoscopy is a visual examination of the ear canal and eardrum using an otoscope (i.e., a hand-held light). Tympanometry consists of placing a small soft rubber-tipped "probe" in the entrance of your ear canal and changing the air pressure to see how the eardrum moves. Acoustic reflex testing consists of the presentation of tonal stimuli at slightly above conversational levels that elicit a middle ear muscle contraction. Audiometry requires you to listen to soft sounds and indicate that you heard by either raising your hand or pushing a button. This series of tests will let us know if you have normal hearing and middle ear function. This will take approximately 20 minutes. The second part of the study involves two standard clinical tests. The first entails placing a small soft rubber tipped probe in the entrance of your ear canal. The probe emits a sound while at the same time measures the ear's response or "echo" to that sound. This test takes approximately 10 minutes. The next test measures electrical potentials recorded from the surface of your skin in response to clicks presented to one ear. I will clean the skin on your forehead and an electrode will be placed here. I will also insert electrodes into your ear canals. You will be asked to relax and remain quiet throughout the testing. During the next part of my study you will sit and listen to noise for 10 minutes. After this amount of time, I will repeat the hearing test, measure the "echo" response, and complete the testing with the electrodes. This will complete the testing on the first day. Within 24 to 48 hours after testing I will ask you to return to repeat a hearing test. This second day of testing will only take approximately 10 minutes.

**What possible harms or discomforts might I experience if I take part in the research?**

There are always risks (the chance of harm) when taking part in research. It has been determined that the risks associated with this research are no more than what you would experience in a normal life. However, some people react to things differently so it is important for you to tell us as quickly as possible if you experience any negative feelings, or feel sick. Participants will not be exposed to excessive sound levels. Participants may feel some fatigue, however, this will be alleviated with frequent timed rest periods or whenever requested.

**What are the possible benefits I may experience from taking part in this research?**

Participants will benefit in receiving a free hearing evaluation. Your willingness to participate in this research will help East Carolina University researchers and other scientists understand the effect of noise on inner ear function in normal-hearing young adults.

**Will I be paid for taking part in this research?**

We will not be able to pay you for the time you volunteer while being in this study.

**What will it cost me to take part in this research?**

It will not cost you any money to be part of the research.

**Who will know that I took part in this research and learn personal information about me?**

To do this research, ECU and the people and organizations listed below may know that you took part in this research and may see information about you that is normally kept private. With your permission, these people may use your private information to do this research:

- Primary Investigator and other members of the research team.
- Any agency of the federal, state, or local government that regulates human research. This includes the Department of Health and Human Services (DHHS), the North Carolina Department of Health, and the Office for Human Research Protections.
- The University & Medical Center Institutional Review Board (UMCIRB) and its staff, who have responsibility for overseeing your welfare during this research, and other ECU staff who oversee this research.

UMCIRB Number: \_\_\_\_\_

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Consent Version # or Date: \_\_\_\_\_  
UMCIRB Version 2012.03.12

Participant's Initials



*Title of Study: The effect of noise exposure on auditory threshold, otoacoustic emissions, and stimulus dependent cochlear potentials*

**How will you keep the information you collect about me secure? How long will you keep it?**

All records related to the study will remain confidential. Participants' names will not be used to identify information or results in scientific presentations or publications. Participants' data will be coded to conceal their identity. Confidentiality will be maintained by assigning each participant a number. Data will be placed in a file(s) and kept in a locked file cabinet(s) in the primary investigator's laboratory and/or office. Only the investigators will have access to the data. A computer file of the data will be maintained on the primary investigator's computer without participants' identity. Participants' identity will be maintained for six years after which any identifying information will be destroyed. Hardcopies will be shredded.

**What if I decide I do not want to continue in this research?**

If you decide you no longer want to be in this research after it has already started, you may stop at any time. You will not be penalized or criticized for stopping. You will not lose any benefits that you should normally receive.

**Who should I contact if I have questions?**

This study does not involve any risk greater than what you experience in everyday life. Therefore, we do not expect you to become sick or hurt as a result of being part of this research. However, people respond differently to things and sometimes accidents do happen. Therefore if you need emergency care, call 911 for help. If possible, take a copy of this consent form with you when you go.

Call the principal investigator as soon as you can. He/she needs to know that you are hurt or ill. Call Alyson Butler at 252-744-6113 or Dr. Andrew Stuart at 252-744-6095.

If you believe you have been hurt or if you get sick because of something that is done during the study, you should call Dr. Andrew Stuart at 252-744-6095 immediately. There are procedures in place to help provide care for you. Costs associated with this care will be billed in the ordinary manner, to you or your insurance company. However, some insurance companies will not pay bills that are related to research costs. You should check with your insurance about this. Costs that result from research-related harm may also not qualify for payments through Medicare, or Medicaid. You should talk to the Principal Investigator about this if you have concerns.

The people conducting this study will be available to answer any questions concerning this research, now or in the future. You may contact the Principal Investigator at 252-744-6113 (days, 8:00 am-5:00 pm).

If you have questions about your rights as someone taking part in research, you may call the Office for Human Research Integrity (OHRI) at phone number 252-744-2914 (days, 8:00 am-5:00 pm). If you would like to report a complaint or concern about this research study, you may call the Director of the OHRI, at 252-744-1971.

**Is there anything else I should know?**

To the best of our knowledge there is nothing else that you should be made aware of.

**I have decided I want to take part in this research. What should I do now?**

The person obtaining informed consent will ask you to read the following and if you agree, you should sign this form:

- I have read (or had read to me) all of the above information.
- I have had an opportunity to ask questions about things in this research I did not understand and have received satisfactory answers.
- I know that I can stop taking part in this study at any time.
- By signing this informed consent form, I am not giving up any of my rights.
- I have been given a copy of this consent document, and it is mine to keep.

UMCIRB Number: \_\_\_\_\_

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Consent Version # or Date: \_\_\_\_\_  
UMCIRB Version 2012.03.12

Participant's Initials

*Title of Study: The effect of noise exposure on auditory threshold, otoacoustic emissions, and stimulus dependent cochlear potentials*

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Participant's Name (PRINT)	Signature	Date
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**Person Obtaining Informed Consent:** I have conducted the initial informed consent process. I have orally reviewed the contents of the consent document with the person who has signed above, and answered all of the person's questions about the research.

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Person Obtaining Consent (PRINT)	Signature	Date
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Alyson K. Butler, B.S.		
Principal Investigator (PRINT)	Signature	Date

UMCIRB Number: \_\_\_\_\_

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Consent Version # or Date: \_\_\_\_\_  
UMCIRB Version 2012.03.12

Participant's Initials

## APPENDIX C: INFORMED CONSENT – PARTICIPANT COMPENSATION

Study ID:UMCIRB 12-002023 Date Approved: 4/27/2013 Expiration Date: 3/17/2014

East Carolina University



### Informed Consent to Participate in Research

Information to consider before taking part in research that has no more than minimal risk.

Title of Research Study: The effect of noise exposure on auditory threshold, otoacoustic emissions, and stimulus dependent cochlear potentials

Principal Investigator: Alyson K. Butler, B.S.

Institution/Department or Division: Department of Communication Sciences & Disorders, College of Allied Health Sciences, East Carolina University

Address: Greenville, NC 27858

Telephone #: 252-744-6095

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Researchers at East Carolina University (ECU) study problems in society, health problems, environmental problems, behavior problems and the human condition. Our goal is to try to find ways to improve the lives of you and others. To do this, we need the help of volunteers who are willing to take part in research.

#### Why is this research being done?

The purpose of this research is to examine the effect of noise on inner ear function in normal-hearing young adults. Inner ear function can be tested noninvasively in humans through electrocochleography (ECochG) and distortion product otoacoustic emissions (DPOAEs). ECochG is an event related potential measuring electrical responses of the inner ear and auditory nerve. DPOAEs are sounds emitted following acoustic stimulation to short/brief duration stimulus. ECochG and DPOAEs provide simple, efficient, and non-invasive objective indicators of healthy inner ear function. **The decision to take part in this research is yours to make. By doing this research, we hope to learn the effect of noise on inner ear function as assessed with ECochG and DPOAEs.**

#### Why am I being invited to take part in this research?

You are being invited to take part in this research because you are a healthy young adult. If you volunteer to take part in this research, you will be one of 32 people to do so.

#### Are there reasons I should not take part in this research?

I understand I should not volunteer for this study if I do not have normal hearing, I am under 18 years of age, or I have been exposed to loud noise/sound in the last 48 hours.

#### What other choices do I have if I do not take part in this research?

You have the choice of not taking part in this research study.

#### Where is the research going to take place and how long will it last?

The research procedures will be conducted in the Department of Communication Sciences and Disorders, College of Allied Health Sciences, East Carolina University, Greenville, NC. You will need to come to room 2310H twice during the study. The total amount of time you will be asked to volunteer for this study is approximately three hours during two days over the next month.

UMCIRB Number: \_\_\_\_\_

Consent Version # or Date: \_\_\_\_\_

UMCIRB Version 2012.03.12

\_\_\_\_\_  
Participant's Initials

**Title of Study:** *The effect of noise exposure on auditory threshold, otoacoustic emissions, and stimulus dependent cochlear potentials*

**What will I be asked to do?**

You are being asked to do the following: First, you will receive a standard clinical audiometric hearing evaluation including tests called otoscopy, tympanometry, acoustic reflex testing, and audiometry (pure tone testing). Otoscopy is a visual examination of the ear canal and eardrum using an otoscope (i.e., a hand-held light). Tympanometry consists of placing a small soft rubber-tipped “probe” in the entrance of your ear canal and changing the air pressure to see how the eardrum moves. Acoustic reflex testing consists of the presentation of tonal stimuli at slightly above conversational levels that elicit a middle ear muscle contraction. Audiometry requires you to listen to soft sounds and indicate that you heard by either raising your hand or pushing a button. This series of tests will let us know if you have normal hearing and middle ear function. This will take approximately 20 minutes. The second part of the study involves two standard clinical tests. The first entails placing a small soft rubber tipped probe in the entrance of your ear canal. The probe emits a sound while at the same time measures the ear’s response or “echo” to that sound. This test takes approximately 10 minutes. The next test measures electrical potentials recorded from the surface of your skin in response to clicks presented to one ear. I will clean the skin on your forehead and an electrode will be placed here. I will also insert electrodes into your ear canals. You will be asked to relax and remain quiet throughout the testing. During the next part of my study you will sit and listen to noise for 10 minutes. After this amount of time, I will repeat the hearing test, measure the “echo” response, and complete the testing with the electrodes. This will complete the testing on the first day. Within 24 to 48 hours after testing I will ask you to return to repeat a hearing test. This second day of testing will only take approximately 10 minutes.

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There are always risks (the chance of harm) when taking part in research. It has been determined that the risks associated with this research are no more than what you would experience in a normal life. However, some people react to things differently so it is important for you to tell us as quickly as possible if you experience any negative feelings, or feel sick. Participants will not be exposed to excessive sound levels. Participants may feel some fatigue, however, this will be alleviated with frequent timed rest periods or whenever requested.

**What are the possible benefits I may experience from taking part in this research?**

Participants will benefit in receiving a free hearing evaluation. Your willingness to participate in this research will help East Carolina University researchers and other scientists understand the effect of noise on inner ear function in normal-hearing young adults.

**Will I be paid for taking part in this research?**

You will be given a \$20.00 gift card for your participation in this study upon completion of testing.

**What will it cost me to take part in this research?**

It will not cost you any money to be part of the research.

**Who will know that I took part in this research and learn personal information about me?**

To do this research, ECU and the people and organizations listed below may know that you took part in this research and may see information about you that is normally kept private. With your permission, these people may use your private information to do this research:

- Primary Investigator and other members of the research team.
- Any agency of the federal, state, or local government that regulates human research. This includes the Department of Health and Human Services (DHHS), the North Carolina Department of Health, and the Office for Human Research Protections.
- The University & Medical Center Institutional Review Board (UMCIRB) and its staff, who have responsibility for overseeing your welfare during this research, and other ECU staff who oversee this research.

UMCIRB Number: \_\_\_\_\_

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Consent Version # or Date: \_\_\_\_\_  
UMCIRB Version 2012.03.12

\_\_\_\_\_  
Participant's Initials

*Title of Study: The effect of noise exposure on auditory threshold, otoacoustic emissions, and stimulus dependent cochlear potentials*

**How will you keep the information you collect about me secure? How long will you keep it?**

All records related to the study will remain confidential. Participants' names will not be used to identify information or results in scientific presentations or publications. Participants' data will be coded to conceal their identity. Confidentiality will be maintained by assigning each participant a number. Data will be placed in a file(s) and kept in a locked file cabinet(s) in the primary investigator's laboratory and/or office. Only the investigators will have access to the data. A computer file of the data will be maintained on the primary investigator's computer without participants' identity. Participants' identity will be maintained for six years after which any identifying information will be destroyed. Hardcopies will be shredded.

**What if I decide I do not want to continue in this research?**

If you decide you no longer want to be in this research after it has already started, you may stop at any time. You will not be penalized or criticized for stopping. You will not lose any benefits that you should normally receive.

**Who should I contact if I have questions?**

This study does not involve any risk greater than what you experience in everyday life. Therefore, we do not expect you to become sick or hurt as a result of being part of this research. However, people respond differently to things and sometimes accidents do happen. Therefore if you need emergency care, call 911 for help. If possible, take a copy of this consent form with you when you go.

Call the principal investigator as soon as you can. He/she needs to know that you are hurt or ill. Call Alyson Butler at 252-744-6130 or Dr. Andrew Stuart at 252-744-6095.

If you believe you have been hurt or if you get sick because of something that is done during the study, you should call Dr. Andrew Stuart at 252-744-6095 immediately. There are procedures in place to help provide care for you. Costs associated with this care will be billed in the ordinary manner, to you or your insurance company. However, some insurance companies will not pay bills that are related to research costs. You should check with your insurance about this. Costs that result from research-related harm may also not qualify for payments through Medicare, or Medicaid. You should talk to the Principal Investigator about this if you have concerns.

The people conducting this study will be available to answer any questions concerning this research, now or in the future. You may contact the Principal Investigator at 252-744-6130 (days, 8:00 am-5:00 pm).

If you have questions about your rights as someone taking part in research, you may call the Office for Human Research Integrity (OHRI) at phone number 252-744-2914 (days, 8:00 am-5:00 pm). If you would like to report a complaint or concern about this research study, you may call the Director of the OHRI, at 252-744-1971.

**Is there anything else I should know?**

To the best of our knowledge there is nothing else that you should be made aware of.

**I have decided I want to take part in this research. What should I do now?**

The person obtaining informed consent will ask you to read the following and if you agree, you should sign this form:

- I have read (or had read to me) all of the above information.
- I have had an opportunity to ask questions about things in this research I did not understand and have received satisfactory answers.
- I know that I can stop taking part in this study at any time.
- By signing this informed consent form, I am not giving up any of my rights.
- I have been given a copy of this consent document, and it is mine to keep.

UMCIRB Number: \_\_\_\_\_

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Consent Version # or Date: \_\_\_\_\_

UMCIRB Version 2012.03.12

\_\_\_\_\_  
Participant's Initials

*Title of Study: The effect of noise exposure on auditory threshold, otoacoustic emissions, and stimulus dependent cochlear potentials*

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Participant's Name (PRINT)	Signature	Date
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**Person Obtaining Informed Consent:** I have conducted the initial informed consent process. I have orally reviewed the contents of the consent document with the person who has signed above, and answered all of the person's questions about the research.

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Person Obtaining Consent (PRINT)	Signature	Date
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Alyson K. Butler, B.S.		
Principal Investigator (PRINT)	Signature	Date

UMCIRB Number: \_\_\_\_\_

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Consent Version # or Date: \_\_\_\_\_  
UMCIRB Version 2012.03.12

\_\_\_\_\_  
Participant's Initials

## APPENDIX D: UNIVERSITY & MEDICAL CENTER INSTITUTIONAL REVIEW BOARD

### RESEARCH APPROVAL FOR CLOSURE



**EAST CAROLINA UNIVERSITY**  
**University & Medical Center Institutional Review Board Office**  
4N-70 Brody Medical Sciences Building · Mail Stop 682  
600 Moye Boulevard · Greenville, NC 27834  
Office 252-744-2914 · Fax 252-744-2284 · [www.ecu.edu/irb](http://www.ecu.edu/irb)

### Closure Notification

From: Biomedical IRB  
To: [Alyson Butler](#)  
CC:  
[Andrew Stuart](#)  
Date: 2/27/2015  
Re: [CR00002619](#)  
2015 Review for UMCIRB 12-002023  
Noise exposure and auditory function

I am pleased to inform you that your request to close this study has been approved on 2/26/2015 .

It is your responsibility to ensure that you retain all research related documents, including the consent form(s), if applicable, for a period of no less than three years. If you have any questions or need for any reason to re-open this research study, please contact the UMCIRB office prior to implementing any research actions.

The Chairperson (or designee) does not have a potential for conflict of interest on this study.

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IRB00000705 East Carolina U IRB #1 (Biomedical) IORG0000418  
IRB00003781 East Carolina U IRB #2 (Behavioral/SS) IORG0000418

